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ACUTE WAR NEUROSIS

SPECIAL REFERENCE TO PAVLOV'S EXPERIMENTAL OBSERVATIONS AND THE MECHANISM OF ABREACTION

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Since the beginning of the war many psychiatrists and neurologists have referred to the importance of "conditioning," in the Pavlovian sense, in the origin and perpetuation of acute war neurosis. Sargant and Slater [1] (1940), reporting on the acute neurotic casualties from Dunkerque, suggested that a process resembling "conditioning" was seen in these patients in a simple form and that the success of physical methods of treatment indicated that physiologic processes played a considerable part in the development of an acute neurosis. Love,[2] in 1942, emphasized the usefulness of a Pavlovian approach to the problems of acute war neurosis, as he had experienced them in the campaigns of the Middle East, and especially during the siege of Tobruk. Symonds,[3] in a recent paper on the human response to flying stress, used Pavlov's [4] observations to discuss methods of inhibition of fear. Methods of "deconditioning" recently acquired fear responses have been the subject of many experiments in World War II. The beneficial effects of emotional abreaction in the acute battle casualty from the intravenous use of barbiturates were also described in the paper by Sargant and Slater [1]; and one of the purposes of the present article is to relate this short-cut psychotherapeutic procedure, developed by Horsley in peacetime, to Pavlovian concepts and to other methods of physical treatment.

In our unit at Sutton Emergency Hospital and elsewhere, we, together with our associates, have treated some 10,000 neurotic casualties, drawn mainly from the services. These patients have included, besides those from Dunkerque, who have already been referred to, casualties from the Battle of Britain and the London blitz, patients from the Mediterranean battlefields and a considerable number also from the battlefields of Normandy. Throughout this period we continued to see neurotic reactions to stress which could be discussed on a basis of Pavlovian conditioning. At the beginning of the fighting in Normandy, Major Howard Fabing, Medical Corps, Army of the United States, suggested to one of us (W. S.) that we try to reexamine these patients in the light of Pavlov's recently translated work "Conditioned Reflexes and Psychiatry." [5] This we have done, and we have also made use of Professor Frolov's [6] book "Pavlov and His School." We have learned much from many conversations with Major Fabing, and some of his ideas must have become inextricably interwoven with ours. We take responsibility for them, however, in their present form, particularly for what we have to say on the subject of ether or amytal abreaction. Some of our observations seem worthy of discussion, since they throw light on the problem of etiology and treatment of neuroses in general and of therapeutic abreaction in particular. But it must be stressed that any theories put forward are tentative and are intended principally to stimulate further research.

PAVLOV'S CONCEPTS

Pavlov visualized the cerebral cortex as a vast, intricate and integrated structure, constantly receiving excitatory and inhibitory stimuli, both from the outside world and from the internal medium. These stimuli have definite areas of reception in the cortex, in which complex conditioned (temporary) reflexes are elaborated and conducted along special paths. The conditioned

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1. Sargant, W., and Slater, E.: Lancet **2**:1, 1940.
2. Love, H. R.: M. J. Australia **2**:137, 1942.
3. Symonds, C. P.: Brit. M. J. **2**:740, 1943.
4. Pavlov, I. P.: Lectures on Conditioned Reflexes: The Higher Nervous Activity (Behaviour) of Animals, London, Lawrence & Wishart, 1928, vol. 1.
5. Pavlov, I. P.: Lectures on Conditioned Reflexes: Conditioned Reflexes and Psychiatry, London, Lawrence & Wishart, 1941, vol. 2.
6. Frolov, Y. P.: Pavlov and His School, translated by C. P. Dutt, London, Kegan Paul, Trench, Trubner & Co., Ltd., 1938.

reflex is distinguished from the unconditioned reflex (or stimulus, or instinct), which is constant and inherent, with an anatomic center in the subcortex or the basal ganglia. The unconditioned reflexes are concerned with food, defense, sex and other fundamental drives. They are the basis for individual adaptation, are essential for the preservation of the species but act only in limited situations and are obviously insufficient for higher adaptation. Finer adjustment, the equivalent of learning from experience, is made by means of the conditioned reflexes. The cortex analyzes and synthesizes external and internal stimuli and regulates the activity of the basal ganglia. In addition to the subcortical and cortical systems, which have arisen in the course of evolution, there is, according to Pavlov, in the human brain a special third system located primarily in the frontal region, which subserves abstraction and speech. Pavlov called the conditioned stimuli of the conditioned reflexes "signals"; and he regarded words as the "equal of signals," or "the second signaling system." This most recently developed function of the human nervous system is also the one most easily disturbed in mental disorder.

Pavlov formulated a series of physiologic laws governing the phenomena of excitation and inhibition—their irradiation, concentration and mutual or reciprocal induction. In a normal personality they show a well balanced equilibrium, within limits. Beyond a certain limit of strength, a stimulus produces not an increased but a decreased effect. When the limit of stimulation has been exceeded, a temporary inhibition follows. During this period, which is accordingly known as the "equivalent," or "paradoxic," phase, a strong stimulus produces a response which is only equal to, or is even smaller than, the response excited by a weak stimulus. The level of stimulation at which this effect occurs is determined, among other things, by the constitutional makeup of the experimental subject.

Pavlov was led by his work on experimental neuroses to classify the types of nervous systems of his dogs in much the same way as Hippocrates classified the temperaments of man. He recognized those in which excitation predominated (the choleric and the sanguine, the excitable and the lively) and those in which inhibition predominated (the phlegmatic and the melancholic, the calm and the inhibitory). The sanguine and phlegmatic types form a central group, of greater stability than the others. Pavlov expressed the belief that a morbid state could be brought about by very strong stimulation, either excitatory or inhibitory, or by the "collision" of excitatory and inhibitory processes. The direction in which breakdown occurs depends on the form of the stress and on the type of the nervous system. By these means he tried to explain the symptoms of neuroses in man, such as hysteria, obsessional states and paranoid ideas. In hysteria there is a predominance of inhibition; the cortical cells become incapable of work as a result of stimuli which would not affect the activity of the normal cortex. The inhibition is thought to be protective, and, depending on its extent, intensity and depth, one sees the phenomena of sleep (widespread irradiation), hypnosis (partial irradiation) and hysteria. The concept of the "weak," "inhibitory" nervous system may be interpreted by the psychiatrist to denote the constitutional weakness of the neurotic person.

The phenomena of the "equivalent," "paradoxic" and "ultraparadoxic" phases, as they have been described by Pavlov in animals, are of particular significance in the present discussion. We have frequently observed somewhat similar forms of behavior among battle casualties. The equivalent and paradoxic phases have already been mentioned. Under still more intensive stimulation, excitatory conditioned stimuli may come to have an inhibitory effect, and vice versa; this is the ultraparadoxic phase. In Pavlov's terminology, such stimuli are called "transmarginal," and the inhibition produced is called "ultraboundary inhibition." In this state the cortical cells become for a time incapable of work, and the animal enters a condition resembling stupor. Excessive stimulation is required to produce this state in the normal cortex, but the threshold is lower in dogs with a weak, inhibitory type of nervous system. Once produced, ultraboundary inhibition may quickly spread over the whole cortex and stop its activity.

A striking example of the ultraparadoxic phase, with the production of ultraboundary inhibition and what Pavlov called "rupture" of the higher nervous activity, was provided by the Leningrad floods of September 1924. These floods penetrated Pavlov's laboratories and subjected his dogs to a terrifying experience. The dogs were in low cells with exit doors close to the floors. Before they could be rescued, the cells were nearly full of water and the dogs could barely keep their heads above water. To get them out of the low exit doors, they had to be dragged under water. After this experience, all recently acquired conditioned reflexes were found to have been abolished in some of the dogs, and it was months before they could be restored. Even thereafter they could be abolished again by any stimulus similar to that of the flood ex-

perience, for instance by a trickle of water running under the door of the cage. According to the Pavlovian theory, the intense excitement caused by the flood had brought about in succession the ultraparadoxic phase, ultraboundary inhibition, rupture of higher nervous activity and abolition of recently elaborated patterns of conditioned behavior.

COMPARISON OF PAVLOV'S EXPERIMENTAL RESULTS AND CLINICAL OBSERVATIONS

Among the patients who came direct to us from the Normandy battlefields, there were, aside from those who showed the usual anxious and depressive symptoms, men with states of simple but profound exhaustion; others with gross, incoordinated, irregular jerking and writhing movements of the limbs and trunk, often accompanied with aphonia or stammer or explosive speech, and yet others in various states of stupor. It was in these patients with hysterical reactions that parallels to Pavlov's experimental observations could most frequently be seen, not only during their period of observation in the hospital but in their behavior of the past as preserved in the field records.

The human nervous system is normally in a state of dynamic equilibrium. But when it is subjected to excessive stimulation, it may pass into a state in which excitation or inhibition predominates and it is incapable of intelligent work. Instances have been reported in which soldiers have broken down into intense excitatory states while in the line, have run at random across no man's land or dashed blindly into machine gun fire. One of our patients advanced twice to help a friend whose leg was blown off but could not bring himself to do it. He then passed into a state of excitement, in which he banged his head repeatedly against a tree and then rushed about wildly, calling for an ambulance. On its eventual arrival, he had himself forcibly strapped down. Another man, after his friend had been killed, tried to rush out to tackle a German tank single-handed; he had to be held down by his comrades and dispatched to a psychiatric center. In these examples, beyond the general state of excitation, there seems to be an inhibition of normal judgment.

States of inhibition appearing in similar circumstances are exemplified by men who passed into a state of stupor or exhibited amnesias or fainting attacks. There were patients who were literally paralyzed with fear. Others passed into states of simple exhaustion; they were usually men of fairly stable personality who had experienced, in addition to mental stress, deprivation of food and sleep. In some cases inhibition seemed to be limited to a smaller area. One patient, for instance, only stammered when there was talk of an officer who had reproved him for cowardice. Loss of voice, followed during recovery by stammering, was common. This frequent disturbance of the "second signaling system" may be due, as Pavlov suggested, to its recent evolutionary development and consequent liability to disturbance by excessive or ultramaximal stimulation. Other forms of focal inhibition were shown by men with a rigid facies, the feeling of a lump in the throat, or a bent back and "weak legs" but without paralysis of the lower limbs. Paralysis of the legs was uncommon, though the gait was often slow. Pavlov described a similar progressive inhibition in his animals submitted to a bombardment of stimuli, starting in the region of the mouth and forward parts of the body and only finally extending to the hindlimbs.

As a rule, there were both focal excitation and focal inhibition. Some patients showed rigidity or inhibition of facial movements or speech combined with tremor or excitation of the hands. Or paralysis of speech might be combined with jerking of the neck. Acute anxiety was often accompanied with inability to swallow. The upper part of the body might shake violently while the lower part was still. A passive or laughing face might be combined with tremors and distorted jerking and writhing movements of the limbs and body.

In these patients with mixed excitation and inhibition, there had been not infrequently sudden changes from one state to the other. One man had been lying trembling in a ditch and feeling paralyzed with fear when his company was about to attack. His officer taunted him with some such remark as "a girl would put up a better show." The man suddenly became wildly excited, shouted to his comrades "Come on, boys!" leaped out of the trench to the attack and "passed out." Other men became panicked and ran about screaming, this phase being followed by sudden total loss of voice. One of our patients collapsed and lay paralyzed and speechless in a village street that was being bombed at the time; but he started suddenly to scream and struggle when he was picked up by his comrades. It is important to note that in a great deal of the abnormal behavior that was observed among these men no motive of gain could be discerned.

These sudden states of total inhibition or collapse which are seen after stress may be examples of Pavlov's ultraparadoxic phase, in which widespread inhibition abolishes normal conditioned

reflexes. Conditions analogous to ultraboundary inhibition were encountered by us, for example, in men who arrived at the hospital in a complete hysterical stupor. Similar states were later induced artificially by stimulation of the patient under ether.

These abnormal states may develop into what Pavlov has termed a dynamic stereotypy, that is, a functional system in the cortex which requires less and less nervous work to maintain it. The repetitive pattern of movements and jerks shown by some of our patients did not yield rapidly to ordinary methods of treatment, such as removal to a hospital and rest, and strong and new stimuli had to be applied to break up the pattern. However, with excessive stimulation under ether, as described later, the condition might rapidly pass off. The stereotypy was not found to be clinically a constant and exactly repetitive pattern, any more than it was in Pavlov's experiments; it was "chaotic" and tended to fluctuate in an irregular fashion.

Somewhat more difficult to describe in terms of Pavlov's theories was a small group of patients whom we saw in our Normandy material. These were men who showed an acute schizophrenic-like syndrome, which we believe on clinical grounds to be an unusual hysterical reaction. Hubert [7] has given a clinical description of similar states which he observed near the front line in the Battle of France. In Pavlov's terminology, this syndrome might be regarded as resulting from an oncoming general inhibition of the cortex, thereby releasing the neighboring subcortex from control; by the mechanism of positive induction there might then ensue a chaotic excitation of the cortex, producing the hallucinations and delusions which are features of this state. These patients usually rapidly responded to deep sedation, which would protect the cortex from subcortical stimulation.

RESPONSE TO TREATMENT

Pavlov's observations may also be related to the results of treatment. He found that under appropriate handling dogs with a "strong," "excitatory" type of nervous system were less liable than the "weak," "inhibitory" type to the development of neurotic states; once a neurosis had been built up, they were, moreover, more likely to respond to early treatment with large doses of bromides. We also have found that men of more stable types of personality are less likely to suffer neurotic states, that when these states occur they are relatively more often exhaustive syndromes and that these men respond frequently to treatment with rather short periods of rest and heavy "first aid" sedation (Sargant [8]).

Among the patients who came to us from Normandy, some had already had three to seven days' treatment with continuous narcosis at advanced psychiatric centers in France; they were evacuated to England when response to treatment was unsatisfactory. Others of the men we received had had only treatment at field dressing stations and were sent to England direct, owing to overcrowding of the psychiatric units in France. The former group were much more heavily loaded with family histories of psychosis or neurosis, and many more of them had had previous nervous breakdowns and had already been seen by army psychiatrists before D day. They could be classified as being of the "weak," "inhibitory" type, and, as Pavlov might have predicted, hysterical reactions predominated.

The physical methods of therapy used by us have been reported in previous articles from this unit. They were continuous narcosis (Sargant and Slater [1]), modified insulin therapy (Sargant and Craske [9]) and combined insulin and narcosis treatment (Sands [10]). Many of these men had remained at duty for some time after the onset of symptoms and had suffered physical deterioration. Losses of weight up to 25 pounds (11.3 Kg.) were recorded. It is perhaps interesting that Pavlov himself commented on the fact that such factors as loss of weight, infections and endocrine disturbances diminished the stability of conditioned responses. We found that patients with stupor and hysterical states of the inhibitory type did best with some form of abreaction before sleep treatment was engaged in. Patients with generalized excitation did well when given sleep treatment immediately. After sleep treatment, both groups of patients went on to receive insulin treatment in order to stabilize recovery and restore weight.

The history of abreaction is a long one. In World War I it was often used with the patient under hypnosis. In World War II the technic of abreaction with barbiturates has been more frequently employed, and this was our usual method until the time of the Normandy campaign. The method does not now require description. A technic of abreaction with ether was developed by Palmer in North Africa, in 1942. As we used it, it may be briefly described as follows: The patient is put into a relaxed state, and a preliminary discussion of events before his break-

7. Hubert, W. H. de B.: Lancet **1**:306, 1941.

8. Sargant, W.: Brit. M. J. **2**:577, 1942.

9. Sargant, W., and Craske, N.: Lancet **2**:212, 1941.

10. Sands, D.: Brit. M. J. **1**:763, 1944.

down is begun. He is then encouraged, under light etherization with an open mask, to put himself back in the situation where his breakdown occurred, or in any situation in which events of strong emotional significance took place, such as being subjected to mortar fire, shelling or bombing. If this is done successfully, the man usually becomes quickly and wildly excited and starts to abreact. The voice becomes louder; the face reddens, and the flush becomes deeper as the emotional release occurs. Some patients became so excited that they had to be held down by one or more doctors.

The intensity of the excitement brought about is generally greater with ether than with amytal, and when the emotional release occurs it is more stormy. Much depends on the way in which the physician handles the situation. With ether the recital of events is more dramatic, and the man behaves as though those same events were happening now. The patient is of set purpose encouraged to cry, to shout and to struggle, as the greater the degree of excitement the better will be the eventual therapeutic results. This artificially induced state of excitement appears to break through localized foci of inhibition and thereby restore a lost memory, bring back speech where there has been aphonia or replace a stammer with normal articulation; we have seen it break through a massive inhibitory state of stupor.

A point of particular interest is that it was not always essential to go over the whole story to get a successful result. It was the high degree of excitement that was desirable, and for this it might be sufficient to bring the etherized patient back in imagination to Normandy and then to say loudly and firmly, "The mortars are coming over again," and "Look, there's a tank coming down the road!"

Some of the best results obtained with ether were in the abolition of a dynamic stereotypy of thought or behavior. Men with localized hysterical jerkings or a persistent anxious rumination about battle experiences did particularly well when the intensity of artificially induced excitement was so great that at its culmination the patient appeared to "collapse" and go into a state of total inhibition for a short time. This was the condition which seemed to us to resemble the ultraparadoxic phase reported by Pavlov in his animals. These stereotypies of behavior, which differ from other hysterical patterns in which the excitatory process is abnormally "labile," showed an abnormal "inertia"; the excitatory process persisted obstinately despite such treatment as continuous sleep, which might have been expected to alter the excitatory process to an inhibitory one. One might say that the ultraparadoxic phase caused a "rupture" of the stereotyped functional system and that recently built-up conditioned behavior was extinguished in a manner similar to the abolition of the conditioned reflexes in Pavlov's dogs after the Leningrad floods.

In some patients we found that when ether abreaction without the appearance of the ultraparadoxic phase had produced little benefit a satisfactory result was obtained when this phase was induced at a second, and later, attempt. Some patients, however, passed readily into this state with a comparatively mild degree of excitement, went through it perhaps repeatedly and did not do well. They showed as a rule severe hysterical reactions and, according to their past histories, pronounced constitutional instability.

It is important to note that ether abreaction did not produce improvement in all types of patients. An already excited patient, without stereotypy or focus of inhibition requiring abolition, might be made worse by the added artificial excitement. Agitated and intensely anxious patients responded better to simple sedation or to abreaction under amytal, in which excitement is damped down as it is released. With patients like these we found it better to begin with a period of sleep treatment and to try abreaction later if required for a residual symptom. Furthermore, if a patient tended to get so excited as to be unmanageable or to pass from excitement into a state of generalized inhibition all too readily, we found it useful to inject sodium amytal intravenously before beginning the etherization. Finally, it was often found difficult to relieve depressed patients by abreaction, although if an emotional storm was successfully induced improvement often resulted. Grinker and Spiegel [11] have recorded a similar lack of success with abreaction under pentothal in patients with hysterical syndromes in which there was a large element of depression. They noted, however, that a few fits induced with metrazol restored the memory and broke up hitherto resistant patterns of neurotic behavior. We, too, have seen a dynamic stereotypy, not responding during continuous narcosis, clear up immediately after a fit induced at the end of the treatment by withdrawal of barbiturates. Psychoanalysts have suggested that therapeutic convulsions are a form of abreaction. Speculation suggests that this view might be correct, that

11. Grinker, R., and Spiegel, J.: War Neuroses in North Africa: The Tunisian Campaign (Jan.-May 1943), New York, Josiah Macy Jr. Foundation, 1943.

the convulsion represents a violent artificially induced excitation, which is followed by ultraboundary inhibition, and that the resulting improvement is due to the "rupture" of a recently acquired conditioned pattern of behavior or thought. A similar speculation could well apply to the phenomena of excitation in the early hypoglycemic stage of insulin shock treatment, when the patient may violently abreact, followed by the temporary phase of total cortical inhibition in the deep coma stage. The beneficial effects obtained with use of the faradic brush in treatment of hysterical syndromes during World War I might also be owed to the intensity of this nonspecific form of excitation.

Caution has to be exercised with these methods of treatment, both in the selection of patients and in the after-care. Some men were not always able to bear without help thought content with a strongly depressive tone which had been brought to the surface by abreaction, and they needed additional psychotherapy and sedation. Men of aggressive personality released under the ether much latent aggression, which could not always be controlled for some time afterward. Violent fluctuations in behavior occurred. A previously inhibited patient might become aggressive and abusive for several hours, until some part of the previous inhibition had been restored. A combination of methods of treatment was frequently necessary.

COMMENT

From the clinical point of view, our most striking observation was the frequency with which we encountered, among some patients with acute neurotic states from the battlefields in Normandy, the series of events represented by the sequence: traumatic experience; abnormal psychiatric state exhibiting stereotypy of behavior or thought; artificially induced state of excitement; sudden collapse of the patient into a condition of total cortical inhibition, and recovery to a more normal psychiatric state. The last three items of this series are in general parlance covered by the term "abreaction." The use of this term dates from the publication of the original paper by Breuer and Freud, in 1895. The use of this process for therapeutic purposes was frequent during World War I, and clinical descriptions reported at the time often end with some such phrase as, "The patient suddenly lay absolutely still," after which comes the statement that the symptom, usually also a form of stereotypy, disappeared. Brown [12] (1920) described the case of a man in whom a tremor of the right hand had developed in battle and who had maintained both the tremor and amnesia for the precipitating incident through two years of treatment, in various military hospitals. During abreaction under light hypnosis he passed into a violent emotional storm, and then "he suddenly lay absolutely still." On recovery from this state, the tremor was no longer in evidence, to the amazement of the patient himself.

For centuries before its psychiatric application, the same method of treatment seems to have been used by evangelists engaged in religious conversion, with the purpose of obtaining an alteration in behavior on the part of their converts. Thus we read in John Wesley's "Journal" [13] for Monday, April 30, 1739:

> We understood that many were offended at the cries of those on whom the power of God came; among whom was a physician, who was much afraid that there might be fraud or imposture in the case. Today one whom he had known many years was the first who broke "into strong cries and tears." He could hardly believe his own eyes and ears. He went and stood close to her, and observed every symptom, till great drops of sweat ran down her face and all her bones shook. He then knew not what to think, being clearly convinced it was not fraud nor yet any natural disorder. But when both her soul and body were healed in a moment, he acknowledged the finger of God.

Grinker and Spiegel, describing the phenomena of abreaction under the barbiturate pentothal sodium, observed in the North African campaign of 1942, reported:

> The terror exhibited . . . is electrifying to watch. The body becomes increasingly tense and rigid; the eyes widen and the pupils dilate, while the skin becomes covered with a fine perspiration. The hands move convulsively, . . . Breathing becomes incredibly rapid or shallow. The intensity of the emotion sometimes becomes more than they can bear; and frequently at the height of the reaction, there is a collapse and the patient falls back in the bed and remains quiet for a few minutes, . . .[11]

Wesley, on Friday, June 22, 1739, wrote:

> While I was speaking one before me dropped down as dead, and presently a second and a third. Five others sunk down in half an hour, most of whom were in violent agonies.[13]

Grinker and Spiegel, describing their results, stated:

> . . . The stuporous becomes alert, the mute can talk, the deaf can hear, the paralyzed can move, and the terror-stricken psychotics become well organized individuals.[11]

Wesley, describing his experience, stated:

> I will show you him that was a lion till then, and is now a lamb; him that was a drunkard, and is now exemplarily sober; the whoremonger that was, who now abhors the very garment spotted by the flesh.[13]

These parallels suggest that phenomena which have something in common have been seen under

12. Brown, W.: Brit. M. J. **1**:142, 1920.

13. Wesley, J.: The Journal of John Wesley, standard edition, edited by N. Curnock, London, Charles H. Kelly, 1909-1916, vol. 2.

a variety of conditions and in a variety of persons but have been brought into relation with quite different philosophic theories. By psychiatrists these phenomena have been produced in individual patients, subjected for the most part to what were taken to be specific psychogenic stimuli. The excitatory and inhibitory phenomena, described by Wesley, among others, as occurring during religious conversion, were obtained by subjecting groups of persons to stimuli of a nonspecific, fear-provoking kind. In their several interpretations, the hand of God has been seen by the religious; the heightening of the transference situation and the release of repressed emotion, by the psychoanalyst; the freeing of the ego, by Grinker and Spiegel. Henderson and Gillespie [14] summarized their views of "narcoanalysis" (Horsley [15]) in the words,

"It is extremely likely that what really is effective in this situation is the doctor's confidence in the treatment." It seems to us that all these interpretations are to some extent inadequate and that one gains in understanding by a consideration in terms of Pavlov's teaching. In these terms the interpretation is purely mechanistic: Excessive stimulation leads to ultraboundary inhibition, a rupture of higher nervous activity and the extinction of recently acquired conditioned reflexes. A point in favor of this view, and against current conceptions of the nature of abreaction, is the observation which has been made both by us and by others, that it is not always necessary to recall to the patient's imagination the precise situation in which the original breakdown occurred; the imaginative recreation of stimuli of a much more general kind may be sufficient.

Pavlov's theories have been disputed by many, but few have disputed the accuracy or reliability of his experimental observations. These observations are, we believe, of great relevance to the problem of formation of neuroses in man. In this paper we have been principally concerned to report, in our turn, our clinical observations. We hope, however, that consideration of both kinds of experiential data in relation to one another may help psychiatrists to take another step in the direction of the comprehensive theoretic synthesis that will one day be attained.

REPORT OF CASES

We give 7 short case records to illustrate some of the more important observations discussed in this paper, especially with respect to our experiments on the mechanism of abreaction. It must be emphasized that these cases are chosen to demonstrate certain points but should be considered in relation to our more general observations. Failure to produce similar improvement in other types of cases is reported in our paper. The occurrence of the improvements recorded does not mean that the patients were necessarily fit to resume front line duties—some went back to lighter duties, and others were eventually discharged from the army to prevent recurrence of the condition. Many of these patients had further insulin therapy, sedation or psychotherapy to stabilize the improvement obtained.

CASE 1.—This case shows the differing effects of sodium amytal and ether in producing excitation during abreaction and the variable results obtained.

Private R. S., aged 26, according to the medical notes from Normandy, was admitted to the Thirty-Second Psychiatric Hospital crying, unable to speak and paralyzed. A psychiatric history, obtained later, showed that his father drank to excess and that his mother was high-strung. The patient was of the nervous, artistic type. He had won a scholarship to an art school when he was 13 and in civilian life had worked as a skilled painter of china. At the age of 19 he had a nervous breakdown, lasting a few weeks, during which he became depressed and unable to face people. He had spent four and a half years in the army as a driver without reporting sick with nerves. In Normandy he had been taken off driving and put into the front line, and the mortar fire and shelling there produced a rapid breakdown. He did not respond to a fortnight's sedation in France and had to be evacuated. On his admission to our hospital, he was still very retarded and apprehensive. He was placed immediately under sleep treatment because he was so upset. After a week, this was followed by modified insulin treatment. But he remained very tense and anxious. He walked slowly, with bent back and rigid facies. An adequate history was still difficult to obtain because of his apprehension and retardation.

At this stage he was given sodium amytal intravenously. Under the effect of the drug he became freer and described being in a static line under mortar fire for eight days. Then he had to take part in an attack in a wood after crossing a river. In the wood he became increasingly nervous and started to shake. When mortars killed several men near him, he lost his voice, burst into tears and became semiparalyzed. Eventually two wounded men had to take him back to an ambulance. "I felt sort of stunned. I lay down crying. I could not speak, but I could cry and utter sounds." Little emotion could be stirred up by this recital, and there was no change in his condition afterward or the next morning.

He was subjected to abreaction with ether on the following afternoon. The same episode was gone over again. This time the recital was accompanied with far greater emotion and excitement. Finally he became

14. Henderson, D. K., and Gillespie, R. D.: Text-Book of Psychiatry, ed. 6, London, Oxford University Press, 1944.

15. Horsley, J. S.: Lancet **1**:55, 1936. Narco-Analysis: A New Technique in Short-Cut Psychotherapy: A Comparison with Other Methods, London, Oxford University Press, 1943.

so excited that he became temporarily confused, tried to tear off the ether mask and overbreathed in a panicky way until the abreaction was stopped. When he got off the couch, an obvious change had occurred. He smiled for the first time and looked relieved. Three days later he said that his symptoms had largely cleared up after the ether abreaction. A week later he still said, "I am a different fellow. I feel fine." A fortnight later there was no return of these symptoms.

Cases 2 and 3 illustrate the breaking up of the symptoms of a "stereotypy" when excitation induced under ether is carried on to the stage of ultraboundary inhibition. In case 2 it will be seen that when excitation under ether was not carried on to the point at which the patient "collapsed" it failed in its purpose. A second ether abreaction, carried on to the ultraparadoxic phase, was successful in the same patient.

CASE 2.—Private L. S., aged 30, was in a confused and tremulous state on admission to the Thirty-Second Psychiatric Hospital. His history showed that he had always been nervous and was especially so during the London blitz. Generally speaking, however, he had been a happy, jolly person before his breakdown in Normandy. He had spent four and a half years in the army as a driver-mechanic and landed in Normandy on D + 17 day. He was in action several weeks, and his symptoms came on gradually. He was given a week's continuous sleep in France but did not respond to this treatment and had to be evacuated. When we saw him, he was depressed and apathetic. He complained of feeling dizzy and being unable to stand the noise of gunfire or airplanes. His thoughts were focused on his friends who had been killed in France. He could not get them off his mind. The scene that bothered him was a horrible one. One of his comrades had a hole blown in his head and died; another had his chin blown off, and a third had blood spurting from his hand.

He was first treated with sedation and modified insulin treatment, but after a fortnight he complained that he felt worse than on admission. He still could not get the scene in which his friends had been killed and injured out of his mind. The first ether abreaction was now carried out. He was taken over the scene that was bothering him, with considerable release of emotion. He said that he thought that his own head was going to be blown off. No ultraparadoxic phase occurred during this abreaction. When he regained consciousness, he cried and said he felt no better. He could "still see it all in his mind."

A second ether abreaction was given at the same session. This time an exciting incident prior to the one he was worrying about was chosen to restimulate excitement. He had been subjected to mortar fire and dive bombing in a churchyard, and it was suggested to him under ether that he was back in that situation. The patient started clawing at the couch, believing he was in a ditch. He was deliberately stimulated by the therapeutist until he passed into a crescendo of fear and excitement. Suddenly he lay dead still. The ultraparadoxic phase had been obtained. On regaining consciousness this time, he was smiling and said, "Everything has gone. It seems different. I feel more open, doctor. I feel better than I did when I came here." When he was asked whether he still remembered his friend's face being blown off, he laughed and said, "I seem to have forgotten all about it. France is not worrying me now." When again asked whether he remembered, he said, "Yes, and the fellow with the hole in his head, but it has lifted from my mind." When asked why this was so, he replied, "I can't explain." He then started to discuss all these incidents freely, without the usual display of emotion. Later in the day he said, "I feel a lot better. It has gone out of my system. I know all about it, but it does not stick in me. It does not affect me in the same way." From this time his symptoms improved greatly.

CASE 3.—Private N. W., aged 24, had been admitted to the Thirty-Second Psychiatric Hospital in Normandy in a stuporous state with aphonia. There, abreaction was carried out under hypnosis, but this led to the development of a pronounced stammer, tics and grimacing. His history showed a fair previous personality, and he had served for three years in the army before the Normandy invasion. He was in action for several weeks, until a shell hit a tree beside which he was lying. Then he lost his voice and his symptoms developed. When first seen by us, he had a coarse, jerking, rhythmic movement of the trunk and upper limbs, and there was a severe stammer. He complained of bad dreams about an incident of mortar fire and an episode in which he had killed a German. All his life he had had an instinctual horror of killing and felt guilty in this act. He was given combined narcosis and insulin treatment for a week, with little improvement. Ether abreaction was then carried out. The patient described how he was out on patrol one night and met a patrol of Germans. He shot one of them. As he described this incident, he got more and more excited, burst out crying and went into a state of total inhibition. When he got up from the couch, his face was relaxed, he had no trace of stammer, and all jerkings had stopped. He continued to improve after this.

Cases 4 and 5 demonstrate the relief of focal cortical inhibition, such as loss of voice or stammer, early in ether excitation. The stereotypy is broken up later by carrying on the excitement to a stage of ultraboundary inhibition.

CASE 4.—Sapper P. B. K., aged 21, had received no specialized psychiatric treatment in Normandy because of the temporary pressure on beds. His history suggested a good army record, but his mother was in a hospital with a nervous breakdown, and his personality showed some anxious and hysterical trends. When we saw him first, he was unable to speak at all and pointed to his lips. He had a gross tremor of the head and upper limbs, the head jerking rhythmically from one side to the other. The shoulders were hunched up, so that the back was kyphotic. On admission he was treated with sedation for his symptoms, but this had little effect. Ether abreaction was then used. Early in the abreaction he started to talk, at first hesitantly. Then his face became red, and gradually he became more emotional. He started to shout loudly and struggle violently as he went over scenes in a mine field in which some friends had been killed. His excitement was stimulated by the therapeutist. Finally he passed into an inhibitory phase. When he regained consciousness and got off the couch, he burst into a broad smile and continued talking freely. His jerkings were less and disappeared entirely in an hour.

CASE 5.—Private C. R. R., aged 22, had been admitted to a field dressing station with difficulty in speaking, mental confusion and complaints of feeling dizzy. His history showed some neurotic traits but no actual breakdown. In the previous year his wife and baby had been

burned to death in an accidental fire, and before that he had lost a younger brother. He had carried on successfully for some weeks under shell fire in Normandy and had broken down when a shell fell near him and killed friends. He had some sedation in Normandy, but when we saw him he had gross jerkings of the limbs and head and a severe stammer. He crouched on the floor at the sound of planes. Continuous sleep for a week improved the general condition, but at the end the stammer and jerking movements continued. Ether abreaction was now used. He described how the dead brought in after his first bombing experience reminded him of his own dead wife and child. He also described being shelled in a chateau. He finally became intensely excited while relating the final incident before his breakdown, when his friends had been killed and wounded. "I ran and ran and lost my voice." This phase of great excitement occurred some time after his stammer had cleared, earlier in the abreaction. It was itself followed by a phase of inhibition. On recovery from this, his speech was normal, and all jerkings had stopped.

CASE 6.—This case illustrates the combined use of sodium amytal and ether to produce a more controlled and effective type of abreaction in a very excited patient and the symptomatic relief obtained when the ultra-paradoxic phase was finally brought about.

Sergeant J. H. T., aged 25, also came from the Thirty-Second Psychiatric Hospital in Normandy. The notes of his record showed that he had broken down after he learned that his mate had been killed. Both had been blown up by a mortar bomb after a week's shelling and mortar fire, and his friend had been badly mangled.

His history was that of a timid child, easily upset by accidents and the sight of blood and fainting easily. His previous army record was good. He had gained rapid promotion as a small arms instructor and had been four years in the service. Prior to his breakdown, the sight of dead bodies in Normandy had always upset him.

His illness first took the form of a depression with retardation and paranoid features. For this, he had been given sedatives in Normandy, with temporary benefit. Then he had become excited, started to stammer and had hysterical hallucinations of battle scenes and ideas of reference. He lost his voice coming over on the boat to England. When we first saw him, he was disheveled and agitated, and there were wild and incoordinated jerkings of the body and arms. He had a "to and fro" rocking movement of the trunk and repeatedly banged his chest with his fist. Sometimes he held a photograph of his fiancée in his hand and at other times he tucked it under his pillow or in his pajama jacket.

When ether abreaction was first tried, it brought back his voice, but he became more overactive and excited than ever. An ultraparadoxic phase did not occur. Some hours afterward his jerking movements were worse, and he had lost his voice again. This time therefore he was given an intravenous injection of sodium amytal to reduce the general excitement and bizarre behavior. It helped in this way but did not restore his voice. A second ether abreaction was now carried out while he was still under the effects of amytal. This brought about a release of much pent-up emotion. He burst into tears, and his voice again returned. Then he began to shout out his story, and he was stimulated to bring about the ultra-paradoxic phase. Suddenly he fell back inert and motionless. On recovery, he was able to speak fairly well and carried on his first rational conversation. Before treatment he had presented a bizarre and almost psychotic picture; now all jerking movements had stopped. Later he was able to write the first letter to his fiancée since his illness. While under observation for the next few days he maintained this improvement.

CASE 7.—This case shows that artificially induced excitation under ether will relieve symptoms of hysterical stupor. There is no need to produce in detail abreaction of a patient's previous battle experiences to achieve this. The case also shows that a detailed recital of battle experiences under hypnosis with sodium amytal may have little effect without the production of excitation.

Sapper J. H. H., aged 43, landed in Normandy on D day and carried on for several weeks under severe stress, until he collapsed. He remembered no more until he found himself in the Thirty-Seventh Psychiatric Hospital in Normandy. He complained of headaches and giddiness. He could not sleep and was tremulous. Sedation was given. He finally arrived back in England on a stretcher, in a state of stupor. He did not answer questions unless pressed to do so, when he might say, "Better," or shake his head. Except for showing fear reactions to aircraft passing overhead, he lay inert all day with his eyes closed. He had to be fed. If he was set up in bed, his head jerked rhythmically.

Soon after admission he was given an injection of sodium amytal intravenously. He gave a full account of himself under the action of the drug. He had been clearing mines at Caen under mortar and shell fire and was much upset at coming across the dead bodies of women and children killed in bombing raids. He was caught in a raid himself, and later several of his friends were blown up and killed by exploding mines. He finally collapsed when he was exposed to machine gun fire. As soon as the effects of the amytal had worn off, he was back in his old state. It was impossible to get anything out of him in the ensuing week. He could not stand and, if spoken to forcefully, might reply, "Better, better, better. . . . ." If he was given a tooth brush, he made constant repetitive movements across his lips. Everything was done in a stereotyped fashion. He was also incontinent, and the only spontaneous activity shown was crouching under the bedclothes if planes passed over the hospital. During another fortnight he failed to respond either to narcosis or to modified insulin treatment. His condition was therefore unchanged three weeks after his admission.

Ether abreaction was now used for the first time. It produced an immediate alteration in behavior. He began to struggle and shout and imagined he was back in Normandy. He went into repeated states of excitement, followed by momentary inhibition. He never went over his experiences in detail, as he had done with amytal. All that was obtained were isolated incidents, rather jumbled up, in his confusion. When the abreaction was stopped, he got up from the stretcher, and from that time he carried on a normal conversation and behaved normally in the ward. A few days later he was again placed under modified insulin treatment to improve his physique. One morning he suddenly relapsed into stupor with only a small dose of insulin while a flight of bombers was going overhead. He did not come out of the stupor on administration of dextrose, either by mouth or by vein. He was therefore given ether again, and it was suggested forcefully to him that he was back at Caen. He became excited very quickly, got up and walked back to the ward. A similar thing happened again a day or two later. This time ether alone did not succeed in bringing him out of the stupor, but stimulation under a combination of ether and amytal was successful. After this his condition became stabilized, and he had no further attacks of stupor in the following month.

SUMMARY

The clinical observations on a group of patients with acute war neuroses seen at the time of the Normandy invasion are compared with the observations of Pavlov on his experimental animals with regard to their symptoms and treatment. Special attention is also given to the mechanism of therapeutic abreaction in the light of Pavlov's work. Case records illustrate some of the points discussed. The concern of this paper is not so much with any particular terminology which has been used to describe our observations as with certain broad mechanistic principles which may underlie a variety of phenomena, hitherto widely separated. Further investigations along these lines may show a rational basis for the greater coordination of various aspects of psychiatric treatment.

Dr. Eliot Slater assisted in the formulation and composition of this paper. Dr. Louis Minski, of the Sutton Emergency Hospital, Surrey, and Dr. Joshua Carse, of Summerdale Emergency Hospital, Chichester, Sussex West, made available treatment facilities, enabling the work to be carried out.

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DISTURBANCES IN SLEEP MECHANISM: A CLINICOPATHOLOGIC STUDY

II. LESIONS AT THE CORTICODIENCEPHALIC LEVEL

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The rarity of disturbances in sleep in patients with pure cortical lesions, as previously reported by us [1] and by others, is in marked contrast to the frequency of their occurrence in patients with lesions involving both the cortex and the diencephalon.

Discrete lesions of the hypothalamus are known to cause interference with normal regulation of sleep. A brief review of the experimental and clinical evidence will be given in a later publication, concerned essentially with lesions at this level. Experimental evidence that lesions at the corticodiencephalic level may be responsible for disturbances in sleep is scanty. Clinical evidence, however, as furnished by the 25 cases in this presentation, and by the reports of other investigators, indicates that lesions at this level, involving either the centers or their pathways, are not of uncommon occurrence. In many of the cases to be discussed it was difficult to determine whether somnolence was the result of the disease of the cortex or of the diencephalon or of both.

REPORT OF CASES

CASE 1.—*Glioblastoma multiforme of the left temporal lobe and basal ganglia; compression and invasion of the infundibular region with pathologic changes in the hypothalamus. Somnolence. Increased intracranial pressure.*

S. F., a girl aged 18 years, slept most of the day and night but could be aroused. There were two episodes of sudden loss of consciousness of twenty-four hours' duration. Craniotomy revealed a neoplasm of the left temporal lobe. The somnolence disappeared, to return later. She was operated on again, but the somnolence persisted.

Neurologic Examination.—There were aphasia, paralysis of the right side of the body with pyramidal tract signs, contraction of the right half of the visual fields and pronounced secondary atrophy of the optic nerves.

Laboratory Data.—The blood urea nitrogen level was normal. The temperature was often 97 F. The cerebrospinal fluid was under a pressure of 280 mm. of water. The spinal fluid contained 4 lymphocytes per cubic millimeter and 145 mg. of protein per hundred cubic centimeters.

Autopsy.—There were destruction and invasion of the left third frontal and temporal convolutions, the basal ganglia and external capsule and part of the hypothalamus, especially the region of the tuber cinereum (fig. 1). All of the diencephalic structures on the left side were compressed. The entire ventricular system and the aqueduct of Sylvius were greatly dilated. The various nerve cells of the left hypothalamus were diminished in number. These cells showed chromatolysis, severe cell changes of Nissl and loss of iron pigment. The nerve cells of the right hypothalamus disclosed slight chromatolytic changes.

Comment.—The lethargy in this case was undoubtedly caused by the compression and invasion of the hypothalamus. It cannot be stated with certainty that involvement of the cortex and the basal ganglia was not a contributory factor.

CASE 2.—*Glioblastoma multiforme of the frontal motor and temporal convolutions, corpus callosum and basal ganglia on the left side, with compression of the hypothalamus and pathologic changes. Drowsiness. Increased intracranial pressure.*

K. N., a man aged 45, gave a history of convulsions, headaches, drowsiness, apathy and projectile vomiting.

Neurologic Examination.—Examination disclosed amaurosis bilaterally, papilledema, diplopia, right flaccid hemiplegia with pathologic reflexes, poor memory, anomia and drowsiness, from which he could be aroused. His vocabulary consisted of "yes" and "no." He could follow simple commands.

Laboratory Data.—The cerebrospinal fluid pressure was 240 mm. of water. The spinal fluid was clear, contained 9 cells per cubic millimeter and had a total protein content of 38 mg. per hundred cubic centimeters. The temperature was occasionally 97 F.

From the Neuropsychiatric Service and the Neuropathological Laboratory of the Montefiore Hospital, and the Neurological Department of Columbia University College of Physicians and Surgeons.

A report on this study, of which the present paper is the second section, was made before the Chicago Neurological Society on May 20, 1943, and before the New York Academy of Medicine, Section of Neurology and Psychiatry, on Feb. 8, 1944. An abstract of the paper, with discussion, was published in the January 1944 issue of the ARCHIVES, page 79.

1. Davison, C., and Demuth, E. L.: Disturbances in Sleep Mechanism: I. Lesions at the Cortical Level, Arch. Neurol. & Psychiat. **53**:399 (June) 1945.

Course of Illness.—After craniotomy and removal of part of the cerebral neoplasm, the patient was in a state of torpor for four days, from which he could be awakened. Then he began to speak spontaneously but perseverated. Later he became somnolent again.

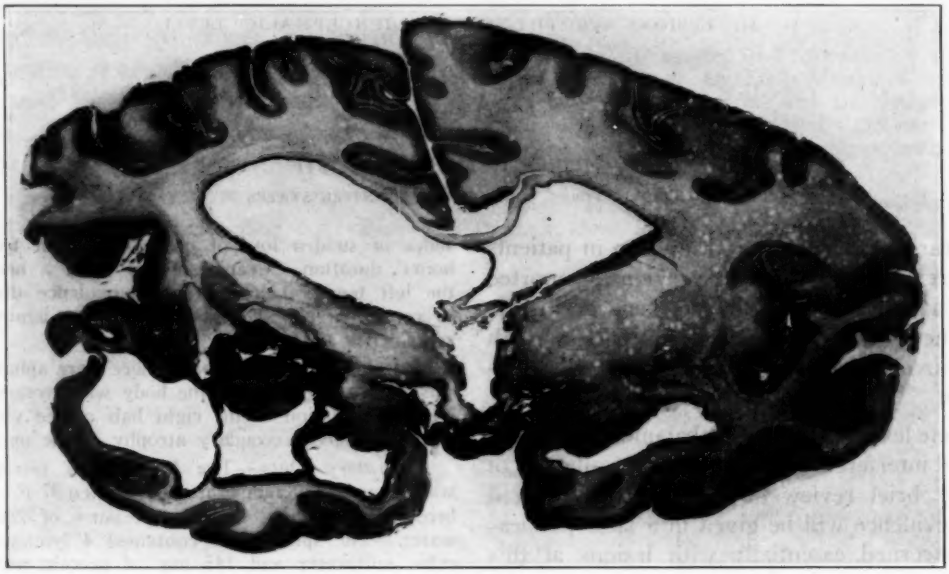

Fig. 1 (case 1).—Glioblastoma multiforme of the left temporal lobe and basal ganglia. Notice invasion of the infundibular region and compression of the hypothalamus.

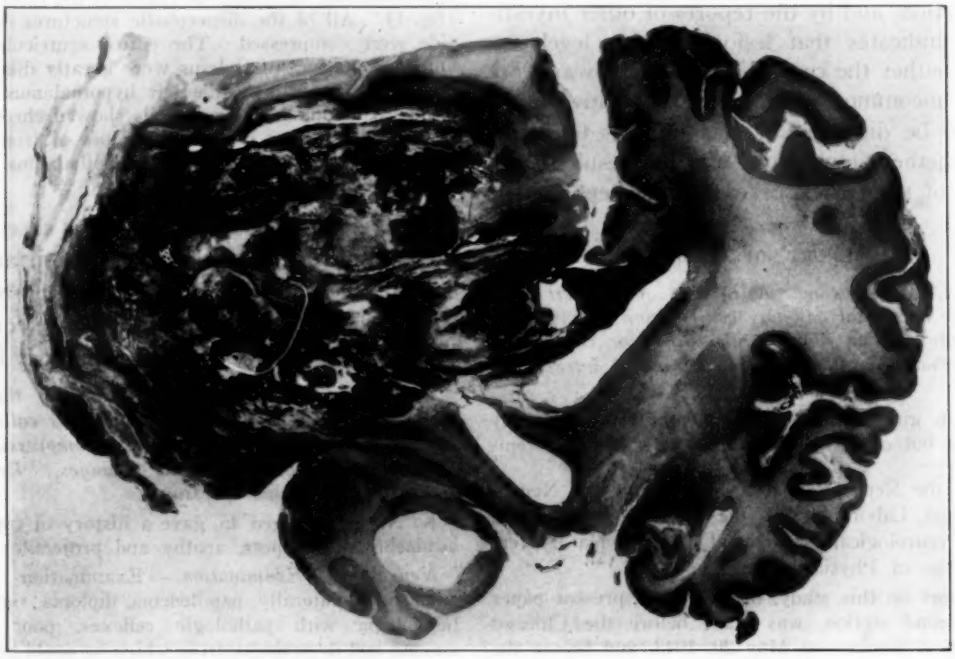

Fig. 2 (case 2).—Glioblastoma multiforme of the left frontal, motor, parietal and temporal convolutions, the corpus callosum and the basal ganglia, with compression of the hypothalamus.

Autopsy.—The left third frontal, motor, temporal and part of the inferior parietal convolution and the left portion of the corpus callosum were replaced with tumor tissue, which was necrotic in places. The left lateral ventricle was constricted and distorted; the third ventricle was dilated. The thalamic nuclei, the striatum and the pallidum on the left side were partly destroyed, and the hypothalamus was compressed (fig. 2). The various hypothalamic nerve cells, especially in the left posterior half, were diminished in number and showed chromatolysis, vacuolation and severe cell changes of Nissl.

Comment.—In this instance the drowsiness was probably caused by the changes in the hypo-

thalamus and by involvement of the cortico-hypothalamic and striohypothalamic pathways.

CASE 3.—*Lymphosarcoma with metastases to the corpus callosum, fornix, hypothalamus and basal ganglia. Korsakoff's syndrome with lethargy. No clinical evidence of increased intracranial pressure.*

C. L., a woman aged 40, had lymphosarcoma, and mental symptoms and lethargy developed.

Neurologic Examination.—There were a typical Korsakoff syndrome, bilateral intention tremor of the extremities and adiadokokinesis of the right upper extremity. The patient was first lethargic and later became stuporous but could always be aroused.

Laboratory Data.—The blood sugar measured 107 mg. and the urea nitrogen 13 mg. per hundred cubic centimeters. The cerebrospinal fluid was not examined.

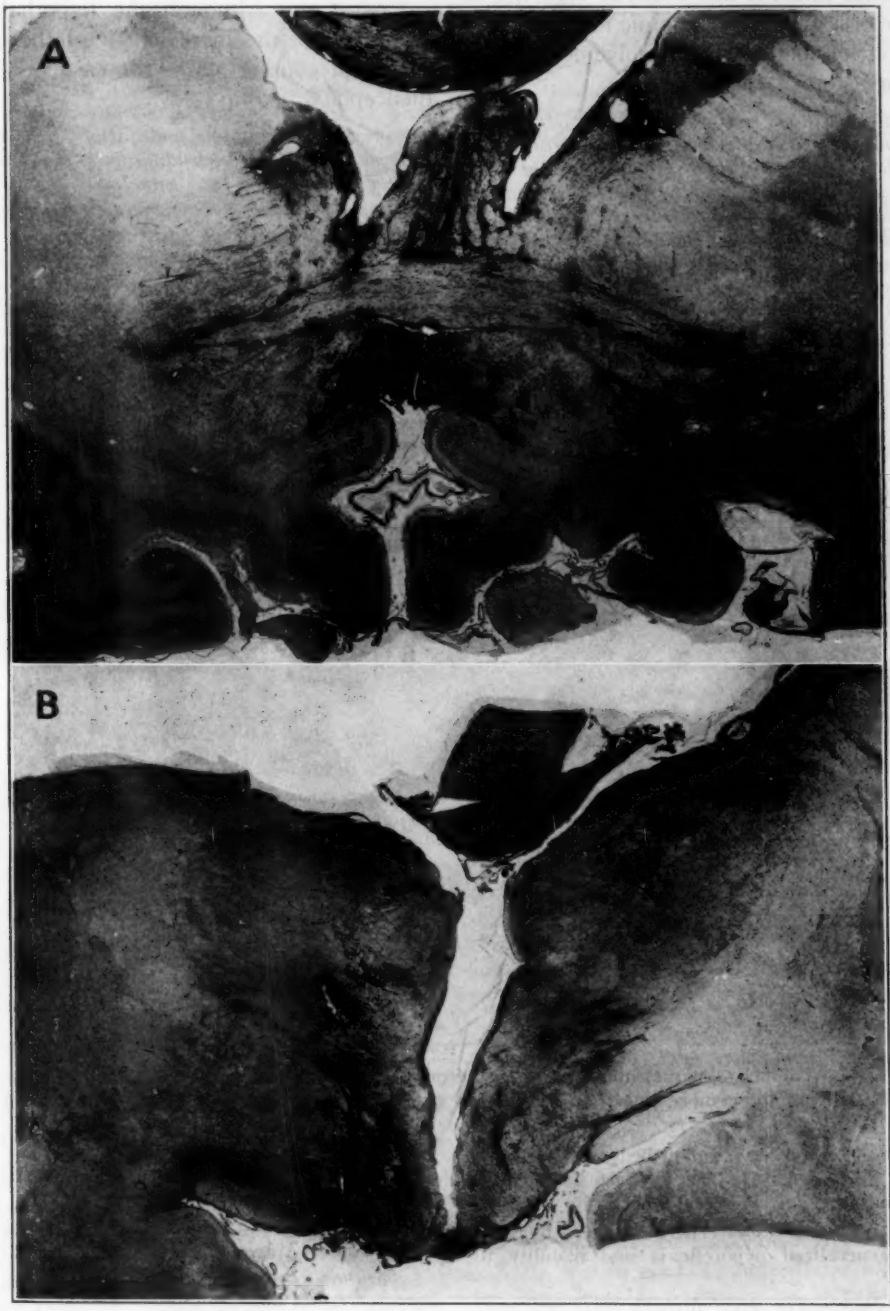

Fig. 3 (case 3).—Lymphosarcomatous invasion of the corpus callosum, the fornix, the preoptic region and the anterior commissura (*A*) and invasion of the pallidum and the hypothalamic region (*B*).

Autopsy.—There were lymphosarcomatous perivascular infiltrations in the corpus callosum, the fornix, the anterior commissures, all of the hypothalamic nuclei and the pallidal segments (fig. 3 *A* and *B*.)

Comment.—This case is placed in the corticodiencephalic group because of the lesions in the corpus callosum and the fornix. The latter is considered a direct corticohypothalamic tract. Were it not for this, the case could be regarded as an example of a pure hypothalamic lesion. There was also striohypothalamic involvement, as a result of invasion of the pallidum.

CASE 4.—*Glioblastoma multiforme of the left frontal and parietomotor convolutions without compression of or pathologic changes in the hypothalamus but with involvement of the basal ganglia. Periods of somnolence. Increased intracranial pressure.*

L. J., a man aged 30, in driving his car, had to stop frequently because of an overwhelming urge to sleep. This somnolence would persist for a few seconds. The attacks continued for five months, with increasing drowsiness, until vision was diminished and headache and vomiting developed. He had to sleep at frequent intervals during the day but could be easily aroused.

Neurologic Examination.—There were bilateral papilledema, generalized hyporeflexia and inability to concentrate.

Laboratory Data.—The urea nitrogen level was normal. Manometric studies revealed an initial pressure of 220 mm. The spinal fluid was xanthochromic, with numerous red blood cells and a 4 plus Pandy reaction.

Course.—An infiltrating glioblastoma multiforme in the left prerolandic area was partially removed, with disappearance of the somnolence. Within six months the somnolence recurred.

Autopsy.—There was a glioblastoma multiforme of the left frontal, motor and orbital convolutions and the corpus callosum (fig. 4). The basal ganglia on the left side were compressed, and the internal capsule, putamen, claustrum, external capsule and entire island of Reil on that side were destroyed. The various hypothalamic nerve cells were normal except for some diminution in heavy iron pigment.

Comment.—Although the hypothalamus was not affected, the involvement of the cortex and the basal ganglia places the case in the corticodiencephalic group.

CASE 5.—*Glioblastoma multiforme of the right frontal and motor regions, extending into the basal ganglia; compression of but no pathologic changes noted in the hypothalamus. Somnolence. Increased intracranial pressure.*

S. L., a man aged 47, had jacksonian seizures and paralysis of the left upper extremity, progressive diminution in vision, headaches and somnolence.

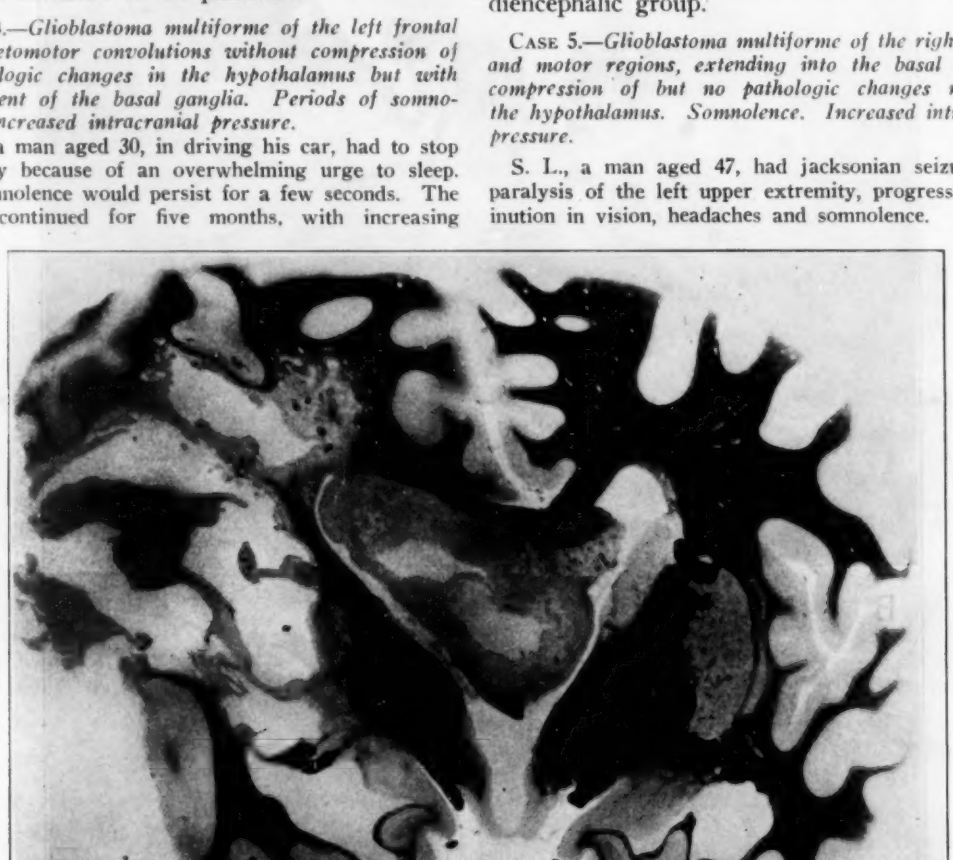

Fig. 4 (case 4).—Glioblastoma multiforme of the left frontal, motor and parietal region, invading the corpus callosum and destroying and compressing part of the basal ganglia. The hypothalamus was not invaded.

Neurologic Examination.—There were left hemiplegia with pathologic reflexes; bilateral atrophy of the optic nerve; slight irregularity of the left pupil, which was larger than the right, and somnolence, from which the patient could be aroused.

Laboratory Data.—Lumbar tap disclosed an initial pressure of 180 mm. of water. All other examinations gave normal results.

Autopsy.—A glioblastoma multiforme involved the right frontal and motor convolutions. The neoplasm extended into the island of Reil, the internal capsule, the putamen and the pallidal segments. The hypothalamus appeared normal.

Comment.—In this case the involved corticodiencephalic and striodiencephalic pathways were probably responsible for the somnolence.

CASE 6.—*Glioblastoma multiforme of the left premotor, motor and parietal regions, with invasion of the basal ganglia and thalamus on the left side; compression of and pathologic changes in the hypothalamus. Attacks of unconsciousness. Increased intracranial pressure.*

S. G., a man aged 34, first experienced jacksonian seizures of the right upper extremity, followed later by attacks of unconsciousness, from which he could be partially aroused. There was bilateral papilledema. After operation and radiation therapy, the disease progressed, with frequent generalized convulsions and loss of consciousness.

Laboratory Data.—Urinalysis revealed a 4 plus reaction for albumin. The blood urea nitrogen measured 13 mg. and the sugar 96 mg., per hundred cubic centimeters. The spinal fluid was xanthochromic; there was a positive Pandy reaction; the total protein content was 257 mg. per hundred cubic centimeters, and the cell count was 35 per cubic millimeter. The pressure was not recorded.

Autopsy.—A tumor in the left premotor, motor and parietal regions involved the corpus callosum, the basal ganglia and the thalamus and compressed the hypothalamic nuclei. The nerve cells of the hypothalamus, especially on the left, showed various pathologic changes.

CASE 7.—*Spongioblastoma polare of the right frontal and motor regions; compression of the striatum but not of the hypothalamus. Attacks of unconsciousness and somnolence. Increased intracranial pressure.*

R. M., a man aged 74, suffered from impaired vision, headaches and attacks of unconsciousness and somnolence. He would lose consciousness and fall to the ground without warning. He could be awakened from some of these attacks but not from others. There were bilateral papilledema and rigidity.

Laboratory Data.—The urine and blood chemistry were normal. Examination of the spinal fluid revealed no cells, 88 mg. of protein per hundred cubic centimeters and an initial pressure of 220 mm. of water.

Autopsy.—A large spongioblastoma was situated in the right third frontal and motor convolutions and extended as far as the external capsule, impinging on the right putamen. The hypothalamus did not appear compressed, and its nerve cells showed no pathologic changes.

Comment.—The hypothalamus in this case did not show pathologic changes. The disturbance of sleep was the result of involvement of the corticodiencephalic or of the striohypothalamic pathways.

CASE 8.—*Abscess of the right frontal, orbital, motor and temporal convolutions, invading the internal capsule, the putamen and part of the pallidum; slight compression of the hypothalamus, with minor changes limited to the preoptic region. Lethargy. Increased intracranial tension.*

C. S., a man aged 23, complained of persistent pain over the right eye and nose following an infection of the upper respiratory tract. He became drowsy but could be aroused.

Neurologic Examination.—There were nuchal rigidity, a bilateral Babinski sign, mimetic movements of the left side of the face and blurring of the left disk margin.

Course.—Spinal tap disclosed 7 cells per cubic millimeter, a total protein content of 41 mg. per hundred cubic centimeters and an initial pressure of 340 mm. of water. The patient was facetious, very talkative and hypomanic. Aspiration of the contents of an abscess from the right frontal lobe was performed, but the lethargy persisted.

Autopsy.—There was an abscess in the region of the frontal, motor and temporal convolutions, the internal capsule, the putamen and part of the pallidum (fig. 5). The hypothalamus was slightly compressed, but the various nerve cells of the hypothalamic nuclei appeared normal, except for a few in the preoptic region.

Comment.—Although the hypothalamus did not show any pathologic changes, because of its slight compression and the involvement of the basal ganglia, there is justification for including this case in the corticodiencephalic group. The role played by the striohypothalamic fibers, as in a few of the other cases in this group, cannot be entirely excluded.

CASE 9.—*Encephalitis lethargica. Diffuse involvement of the cortex, basal ganglia and diencephalon. Periods of somnolence. No evidence of increased intracranial pressure.*

P. H., a boy aged 7 years, had fever and periods of drowsiness. Later there appeared generalized myoclonic movements and difficulty in speech.

Neurologic Examination.—There were choreiform and myoclonic movements of the whole body, especially the face and the upper extremities. The patient was drowsy but could be aroused. The pupils reacted to light and in accommodation.

Laboratory Data.—Spinal tap disclosed an initial pressure of 150 mm. There were no cells, and the total protein measured 41 mg. per hundred cubic centimeters. The blood chemistry was normal. The temperature varied between 97 and 101 F.

Autopsy.—A widespread encephalitic process extended throughout the central nervous system, including the cortex, the basal ganglia, the thalamic and hypothalamic nuclei (fig. 6), the mesencephalon and the metencephalon.

Comment.—Although the lesions were diffuse, those in the hypothalamus undoubtedly played the most important role in the causation of somnolence.

CASE 10.—*Multiple cerebrovascular lesions involving branches of the middle cerebral arteries; lesions in the hypothalamus and basal ganglia. Somnolence. No evidence of increased intracranial pressure.*

S. Z., a man aged 69, suffered for four years from left hemiplegia and spontaneous laughing and crying. Toward the end of the fourth year, extreme lethargy appeared, from which he could be aroused. He lost interest in everything and wished only to sleep. When aroused, he would respond to questioning with outbursts of crying. Later, somnolence became more prolonged and profound.

Neurologic Examination.—There was left hemiparesis with bilateral pyramidal tract signs, palsy of the right side of the face of central type and impairment of mental functioning.

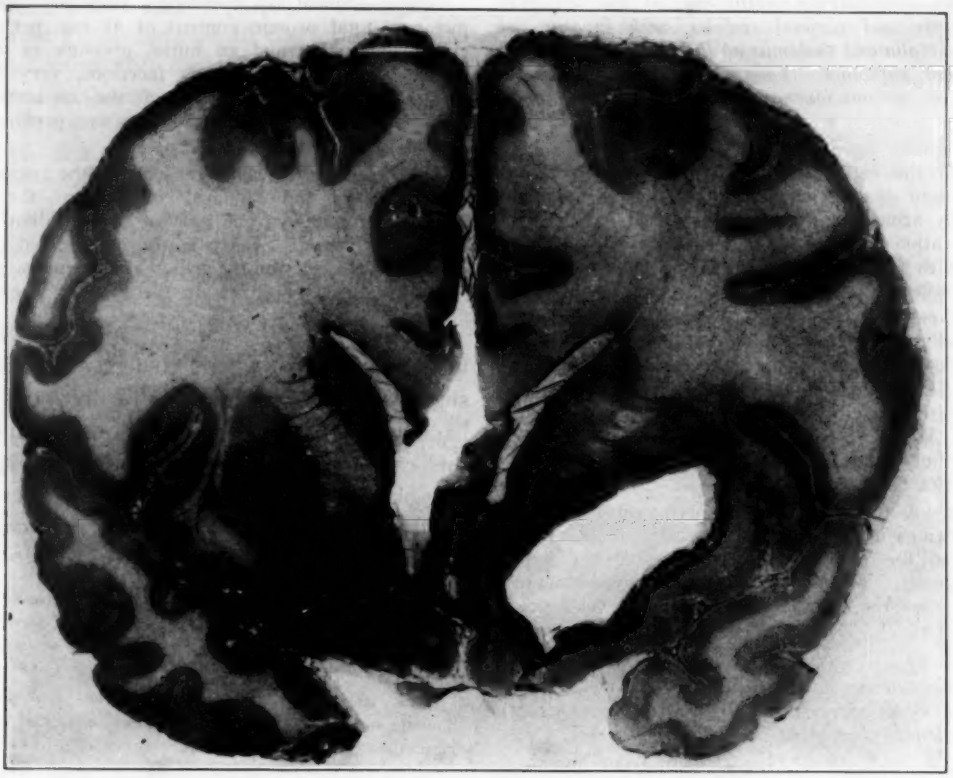

Fig. 5 (case 8).—Abscess of the right frontal and orbital convolutions, compressing and slightly invading the putamen and part of the pallidum, with compression of the preoptic region.

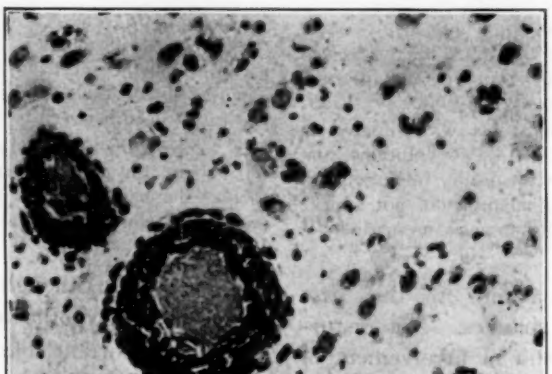

Fig. 6 (case 9).—Perivascular infiltration in the diencephalon in a case of encephalitis lethargica.

Laboratory Data.—The blood chemistry was normal. The spinal fluid contained 13 cells, all lymphocytes, per cubic millimeter; the Pandy reaction was negative, and the initial pressure was 120 mm. The temperature ranged from 97 to 98 F., occasionally falling to 96 and once to 95 F.

Course.—The patient had episodes of explosive weeping, although generally he appeared cheerful and happy. His lethargy deepened, and he lost interest in his surroundings. He finally became cataleptic.

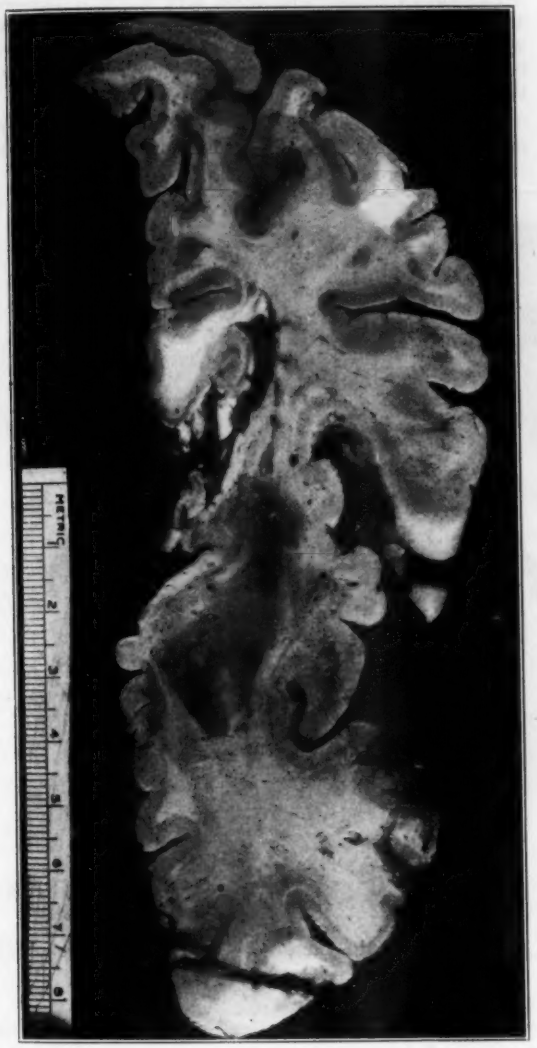

Fig. 7 (case 10).—Multiple cerebrovascular lesions involving branches of the middle cerebral arteries, with lesions of various convolutions, the internal capsule, the basal ganglia and the hypothalamus.

Autopsy.—There were several areas of softening along the distribution of both middle cerebral arteries with involvement of various convolutions, the internal capsule and the striatum (fig. 7). Throughout the basal ganglia and the hypothalamus, there was calcification of the vessels with areas of devastation. In the hypothalamus, some of the nerve cells of the nucleus paraventricularis, the nucleus supraopticus, the nucleus reuniens and the tuber cinereum were destroyed by this process.

Comment.—The somnolence was probably the result of hypothalamic lesions. Corticohypothalamic or striohypothalamic involvement, however, cannot be ruled out.

CASE 11.—*Diffuse syphilitic encephalitis involving the cortex and the diencephalic nuclei. Somnolence. No evidence of increased intracranial pressure.*

S. A., a man aged 72, presented impairment in memory for past and recent events, disorientation and somnolence.

Neurologic Examination.—The patient was semistuporous but responded to noxious stimuli. The pupils reacted to light and in accommodation.

Laboratory Data—The blood urea nitrogen measured 30 mg. per hundred cubic centimeters; the Wassermann reaction of the blood was 4 plus and the Kahn reaction 2 plus. The Wassermann reaction of the spinal fluid was 4 plus; the gum mastic curve was 555442100. The recordings of the spinal fluid pressure were not given, but it was stated that they were normal.

Autopsy.—There was generalized atrophy of the convolutions, particularly the frontal. A diffuse inflammatory process was present in the cortex and the diencephalic nuclei. Some of the nerve cells of the hypothalamic nuclei showed pathologic changes, such as shrinkage, chromatolysis, loss of iron pigment and complete destruction.

CASE 12.—*Glioblastoma multiforme, extending from the right frontal to the occipital convolutions; compression of the basal ganglia and hypothalamus, with pathologic changes in the nerve cells. Episodes of drowsiness. Increased intracranial pressure.*

C. C., a man aged 37, had convulsive seizures with loss of consciousness. Later developments included personality changes, loss of libido and drowsiness. He would continually fall asleep at any time during the day, sleeping for irregular periods, but he could be aroused on questioning. There then developed failing vision, with bilateral choked disk, projectile vomiting, bilateral pyramidal tract signs and sensory disturbances on the left side. Craniotomy revealed a glioblastoma multiforme in the right frontoparietal area. The drowsiness increased after the operation. The temperature was often 97 F. and once 96.6 F.

Laboratory Data.—The cerebrospinal fluid was under a pressure of 240 mm.; it contained 15 cells per cubic millimeter and 80 mg. of protein per hundred cubic centimeters.

Autopsy.—The gray and white matter on the right side, from the frontal to the occipital convolutions, were infiltrated with a glioblastoma multiforme. In sections through the diencephalic nuclei, in addition to destruction of the respective convolutions, there was involvement of the putamen, the pallidum, the internal and external capsules, the insula and part of the thalamic nuclei on the right side. The hypothalamic nerve cells on this side showed shrinkage, disintegration of Nissl substance and pronounced loss of iron pigment.

Comment.—The sleepy state in this instance was probably caused either by involvement of the corticodiencephalic and striohypothalamic pathways or by the compression of the hypothalamus.

CASE 13.—*Glioblastoma multiforme of the left frontal, temporal and parietal convolutions and basal ganglia;*

compression of the posterior hypothalamus. Recurring lethargy. Increased intracranial pressure.

L. S., a man aged 54, in addition to many neurologic symptoms, had sudden episodes of lethargy, from which he could be aroused. These attacks were associated with a slow pulse of 60 per minute. The patient's condition improved, and his lethargy disappeared. He was then considered to have chronic encephalitis. Six weeks later, however, there was a return of the lethargy, followed by semistupor. There was bilateral papilledema. Spinal tap disclosed an initial pressure of 150 mm., and there was an increase in globulin.

Autopsy.—A tumor was found in the left second and third frontal convolutions. Sections through the insula and basal ganglia revealed two tumors—one situated in the left temporal and parietal lobes and the other in the white mater directly above it, involving

especially in the posterior half. Somnolence. No evidence of increased intracranial pressure.

K. D., a man aged 52, frequently fell asleep after supper, a most unusual procedure for him. Later, marked changes in behavior, confusion, deliriousness and drowsiness were noted.

Neurologic Examination.—The patient was in stupor, from which he could be aroused with difficulty. There were hyperactive reflexes, normal fundi and slightly irregular pupils, which reacted sluggishly to light.

Laboratory Data.—The blood urea nitrogen measured 19 mg. per hundred cubic centimeters. The spinal fluid was clear and contained no cells; the total protein content was 39 mg. per hundred cubic centimeters, and the initial pressure was 120 mm. of water.

Autopsy.—A glioblastoma multiforme had destroyed practically all of the right temporal convolutions and

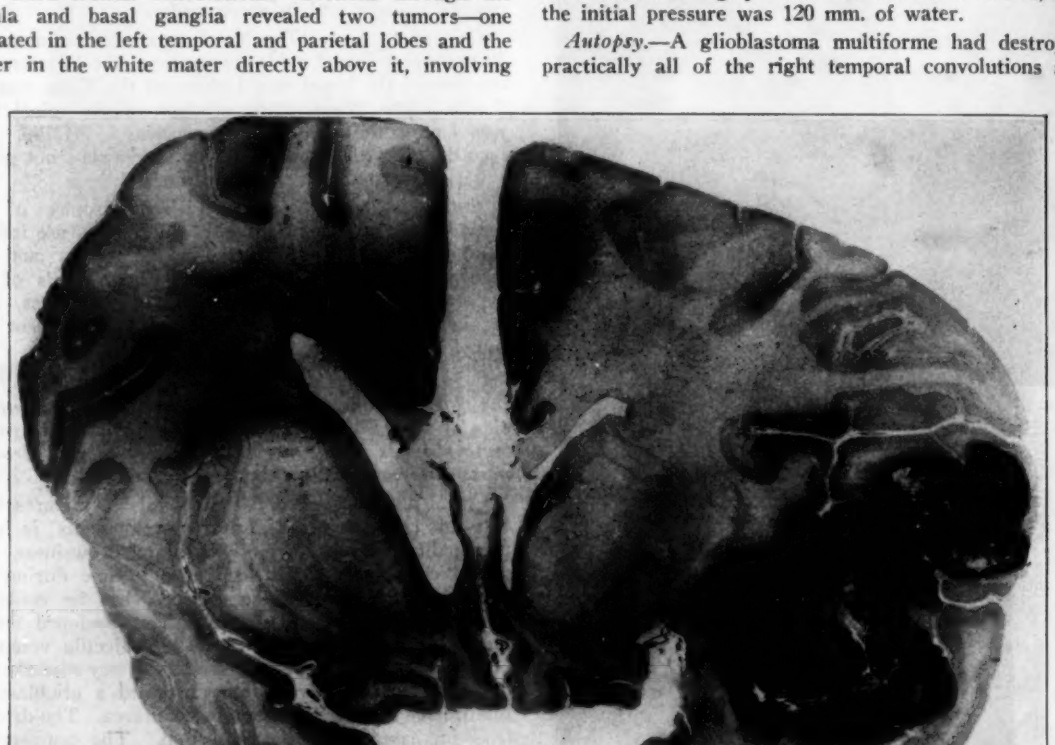

Fig. 8 (case 14).—Glioblastoma multiforme of the right temporal lobe, with compression of the basal ganglia and the hypothalamus.

the putamen, the globus pallidus and the island of Reil. The various hypothalamic nuclei on the left were compressed and distorted, and their nerve cells, especially in the posterior half, showed all types of pathologic changes, such as complete destruction, shrinkage and loss of chromatin and of heavy iron pigment.

Comment.—In this instance, the somnolence and other symptoms could easily be accounted for by the frontal and temporal neoplasm, which extended into the basal ganglia and partially compressed the various hypothalamic nuclei, especially those of the posterior half.

CASE 14.—*Glioblastoma multiforme of the right temporal lobe; compression of the basal ganglia and hypothalamus with pathologic changes in its nerve cells,* part of the insula. There was slight compression of the diencephalon and the basal ganglia on the right side (fig. 8). The hypothalamic nerve cells, especially of the right posterior half, were diminished in number and showed chromatolysis, loss of pigment granules and severe cell changes of Nissl. The nerve cells on the left side were better preserved.

Comment.—Although the tumor was limited mainly to the cortex, there was also compression of the diencephalon and the basal ganglia, with pathologic changes in the posterior half of the hypothalamus to account for the drowsiness. This patient was one of the few whom it was difficult to arouse.

CASE 15.—*Astroblastoma of the left motor and parietal regions; compression of the basal ganglia and hypothalamus, without changes in the nerve cells of the hypothalamus. Lethargy, which cleared up after removal of the tumor; recurrence later. Increased intracranial pressure.*

K. I., a man aged 50, gave a history of headaches and spells of confusion and drowsiness, from which he could be aroused.

Neurologic Examination.—Papilledema was present bilaterally; the left pupil was smaller than the right, and there was right homonymous hemianopsia, with sparing of the macula.

Course.—A craniotomy was performed, and an astroblastoma was removed from the left temporoparietal region, after which the lethargy cleared up for a few weeks but recurred later.

Laboratory Data.—Examination of the spinal fluid disclosed 2 cells per cubic millimeter, a positive Pandy reaction, a total protein content of 58 mg. per hundred cubic centimeters and an initial pressure of 360 mm. The blood chemistry was normal, and the other data were not remarkable.

Autopsy.—An extensive neoplasm destroyed part of the white matter from the motor to the end of the parietal region on the left side. The basal ganglia and the hypothalamic structures on the left were slightly compressed. There was, however, no evidence of any pathologic changes in the nerve cells of the hypothalamus, except for some loss in iron pigment granules.

Comment.—Although the tumor was limited to the motor and parietal regions, there was some compression of the basal ganglia and the hypothalamic nuclei on the left side, without any evidence of changes in the nerve cells. It is possible that pressure on the striohypothalamic pathways might have led to the state of lethargy.

CASE 16.—*Carcinoma of the lung with metastases to the right parieto-occipital region; compression of the basal ganglia and the posterior half of the hypothalamus with changes in its nerve cells. Lethargy. No evidence of increased intracranial pressure.*

A. A., a woman aged 37, gave a history of diplopia, frontal headaches, nonprojectile vomiting, myoclonic twitching on the left side of the body, numbness of the left hand and lethargy, from which she could be aroused. At this time, a diagnosis of lethargic encephalitis, was considered.

Neurologic Examination.—Examination disclosed left hemiparesis with pathologic reflexes, left hemihypalgesia, bilateral ptosis, convergent squint, total external ophthalmoplegia, irregular pupils, which did not react to light and in accommodation, anesthesia of the left cornea, masked facies and difficulty in opening the jaw.

Laboratory Data.—A spinal tap showed clear fluid under normal pressure. The blood chemistry was normal.

Autopsy.—The right parietal and occipital lobes were replaced by a large cystic tumor, which compressed and destroyed part of the putamen and the globus pallidus. The hypothalamus on the same side was compressed. The various hypothalamic nerve cells, especially in the posterior half, were diminished in number and showed loss in chromatin and absence of iron pigment.

Comment.—The lethargy in this case was at first considered to be the result of lethargic encephalitis, but at necropsy it was demonstrated to have been caused by a neoplasm involving the cortex and the basal ganglia and compressing the hypothalamus. As in some other cases, the nuclei of the ocular nerves were involved.

CASE 17.—*Carcinoma of the breast with diffuse metastases in the central nervous system, including the basal ganglia and the hypothalamus. Lethargy. Increased intracranial pressure.*

G. E., a woman aged 36, had a neoplasm of the breast, which was removed. Three years later she complained of dizziness, vomiting and a desire to sleep all the time.

Neurologic Examination.—The patient was somnolent, from which state she could be aroused with difficulty, but she responded readily to questioning. The optic disks were blurred.

Laboratory Data.—The cerebrospinal fluid was not examined. The blood chemistry was normal.

Autopsy.—The diencephalon, basal ganglia, mesencephalon, cerebellum and occipital convolutions were infiltrated with metastases. The various hypothalamic nuclei were also invaded by the neoplasm, and their nerve cells showed all types of pathologic changes.

CASE 18.—*Astrocytoma of the right frontal, motor, parietal, temporal, hippocampal and occipital convolutions, with compression of the hypothalamus. Somnolence. Increased intracranial pressure.*

M. P., a woman aged 54, experienced headache, blurred vision, vomiting and vertigo, followed later by loss of consciousness, from which she could be aroused. There were papilledema, ptosis of the left eyelid, left hemianopsia and other neurologic signs irrelevant to the somnolence. After a craniotomy in the right parietotemporal region, there was an increased tendency to somnolence.

Laboratory Data.—The urine and the blood chemistry were normal. The spinal fluid showed an initial pressure of 300 mm.

Autopsy.—An astrocytoma involved the right frontal, motor, parietal, temporal, hippocampal and occipital convolutions. The tumor extended through the region of the splenium of the corpus callosum into the hippocampus, the fusiform gyrus and the occipital convolutions (fig. 9). Part of the lateral and inferior hypothalamic nuclei on the right side were compressed by the neoplasm (fig. 9). Some of their nerve cells showed pallor and chromatolysis.

CASE 19.—*Glioblastoma multiforme of the left temporal lobe, compressing the caudal and lateral parts of the hypothalamus. Recurring lethargy. Increased intracranial pressure.*

J. A., a man aged 38, suffered from severe frontal headache and sleepiness, from which he could be aroused. There was bilateral papilledema. His temperature was normal, and his pulse 60 per minute. A history of head trauma five months previously was elicited. Exploration for a subdural hematoma revealed a neoplasm.

Laboratory Data.—The spinal fluid was under an initial pressure of 360 mm. of water and contained 3 cells per cubic millimeter. The serologic reactions were positive, and the colloidal gold curve was of first zone, dementia paralytica, type.

Autopsy.—There was a tumor extending from the left temporal to the occipital convolutions. Part of the left caudal and lateral portions of the hypothalamus were compressed. The hypothalamic nerve cells were diminished in number and appeared "washed out." Occasional destruction of nerve cells was also noted.

CASE 20.—*Glioblastoma multiforme of the right frontal, motor and parietal convolutions; slight compression of and pathologic changes in the hypothalamus. Somnolence. Increased intracranial pressure.*

tion of 2 plus. The results of all other laboratory studies were noncontributory.

Autopsy.—A glioblastoma multiforme involved the right frontal, motor and part of the parietal convolutions. The hypothalamus was compressed, and the various hypothalamic nerve cells, especially on the right, showed ischemia, chromatolysis or severe cell changes of Nissl.

CASE 21.—*Glioblastoma multiforme of the left parieto-occipital region, compressing the posterior part of the*

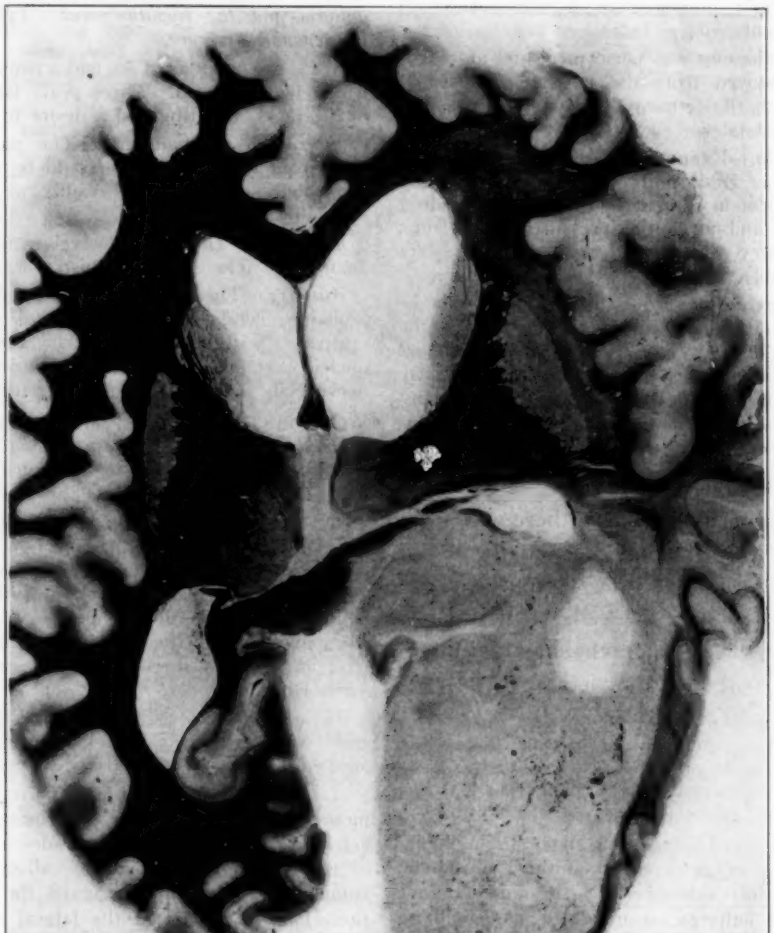

Fig. 9 (case 18).—Astrocytoma of the right occipital, hippocampal and temporal convolutions with compression, especially of the right hypothalamus.

S. L., a man aged 48, had progressive paralysis of the left arm, associated with jacksonian motor and sensory seizures. There were also headaches, twitching of the eyelids and dimness of vision. After a craniotomy, the patient became somnolent but could be aroused. In addition to other neurologic findings, there were bilateral atrophy of the optic nerve and slight irregularity of the left pupil, which was larger than the right.

Laboratory Data.—Spinal puncture showed an initial pressure of 450 mm. of water, a protein level of 78 mg. per hundred cubic centimeters and a Pandy reac-

hypothalamus. Insomnia, later followed by somnolence. Increased intracranial pressure.

V. M., a woman aged 39, complained of headaches, dimness of vision, memory defects, insomnia, vomiting, apathy and drowsiness. There was bilateral papilledema. The right pupil was larger than the left and reacted slightly less to light. Impairment of right conjugate deviation was evident. A cystic tumor was removed from the left occipital lobe at operation. The patient became progressively more drowsy and apathetic but could be aroused.

Laboratory Data.—The spinal fluid was under an initial pressure of 320 mm. of water.

Autopsy.—There was a hemorrhagic tumor in the region of the left parieto-occipital area, destroying part of the pulvinar, the entire centrum ovale and part of the white and gray matter of the fusiform gyrus and hippocampus. The hypothalamus was compressed, and the hypothalamic nerve cells, especially on the left and posteriorly, showed pathologic changes.

CASE 22.—*Suprasellar meningioma, without invasion of the sella turcica but compressing the frontal, orbital and cingular gyri and the hypothalamus. Lethargy. No evidence of increased intracranial pressure.*

K. E., a woman aged 50, suffered from sleepiness and drowsiness. She would sleep for three days continuously unless awakened. Later, there developed visual impairment, which progressed to complete blindness.

Neurologic Examination.—The patient was completely disoriented, and her mood varied between joviality and violence. She slept and yawned most of the time but could be aroused. There were jargon aphasia, bilateral atrophy of the optic nerve, with complete amaurosis, and generalized hyperreflexia. The temperature ranged from 97 to 98 F.; once it was 96.6 F. There were no endocrine disturbances.

Laboratory Data.—The serologic reactions of the blood and spinal fluid were negative. The spinal fluid was clear, contained 3 cells per cubic millimeter and showed an initial pressure of 80 mm. of water. The blood chemistry was normal.

Autopsy.—A large tumor, the size of a small orange, extended caudally from the rostral end of the anterior fossa to the sella turcica, compressing the optic nerves, the optic chiasm, the olfactory tracts and the floor of the third ventricle (fig. 10). The structures on the inferior surface of the brain, from the tip of the frontal pole to the peduncles, including the gyrus cingulus, were distorted and compressed. The tumor did not invade the sella turcica but compressed the entire hypothalamus. Most of the hypothalamic nerve cells showed chromatolysis, shrinkage, severe nerve cell changes of Nissl and loss of pigment granules. The ventricular system did not show significant changes.

Comment.—This case could be placed with the cases of hypothalamic lesions were it not that some of the cortical convolutions, especially the orbital gyrus and the gyrus cingulus, were also compressed. It is doubtful whether the pituitary played any role in the causation of somnolence since the sella turcica was not invaded. There was no evidence of increased intracranial pressure.

CASE 23.—*Adenoma of the pituitary gland, with compression of the hypothalamus and the temporo-orbital convolutions; invasion of the hippocampus. Lethargy. Increased intracranial pressure.*

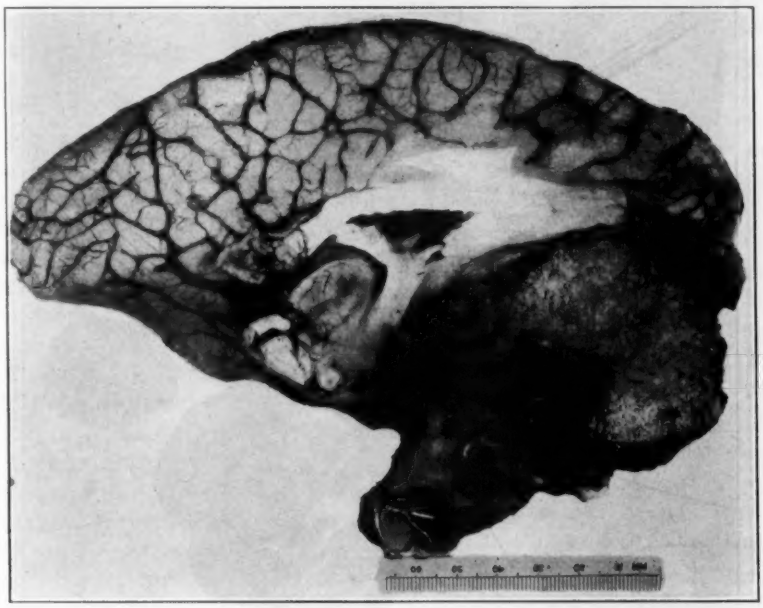

Fig. 10 (case 22).—Suprasellar meningioma compressing the frontal, orbital and cingular gyri and the hypothalamus.

A. G., a man aged 48, complained of loss of libido. A diagnosis of tumor of the pituitary was made. After operation, there appeared visual hallucinations, blindness and drowsiness.

Examination disclosed a blood pressure of 90 systolic and 50 diastolic; small testicles; pale, soft skin; absence of hair on the breast and in the axilla and sparse pubic hair, and amaurosis, with bilateral atrophy of the optic nerve. There were frequent convulsive seizures. The patient was lethargic but could be aroused. Later, confusion and negativism appeared.

Laboratory Data.—The urine was normal. The blood urea nitrogen measured 5.6 mg. and the sugar 85 mg. per hundred cubic centimeters. The spinal fluid contained 9 cells per cubic millimeter and 60 mg. of protein per hundred cubic centimeters, with a negative Pandy reaction and an initial pressure of 60 mm.

Autopsy.—A large adenoma of the pituitary was situated between and compressed the temporal lobes,

the orbital convolutions and the hypothalamus (fig. 11). A small nodule invaded the left hippocampus (fig. 11). All the hypothalamic nerve cells showed pathologic changes.

Comment.—This patient's drowsiness was the result of compression of the hypothalamus, although the effects of cortical involvement cannot be excluded.

CASE 24.—*Suprasellar meningioma, compressing the orbital and cingular gyri and the hypothalamus. Somnolence. Increased intracranial tension.*

S. R., a woman aged 61, when examined showed drowsiness and stupor, from which she could be aroused, pyramidal tract signs on the left, diminution of smell on the right, bilateral papilledema and mental changes. There were no endocrine disturbances except for myxedema. At operation a large meningioma was removed from the right olfactory groove. A spinal tap was not done.

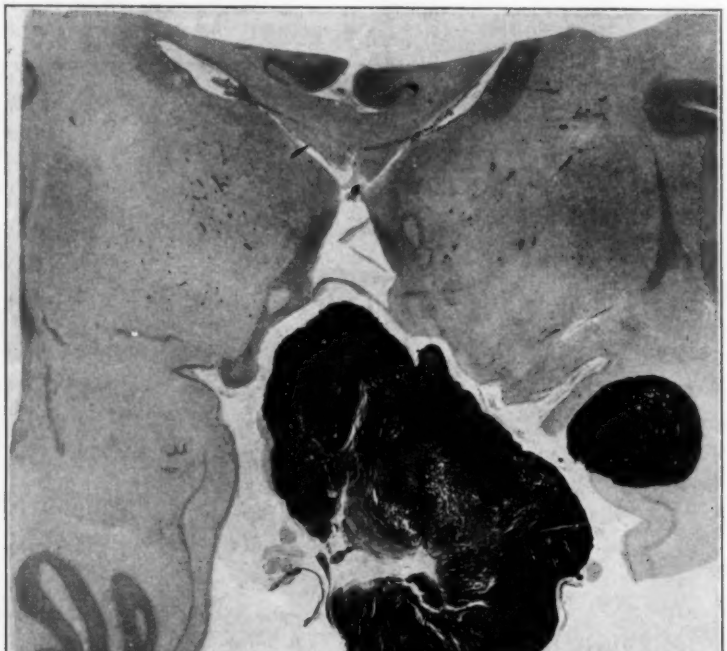

Fig. 11 (case 23).—Adenoma of the pituitary compressing the hypothalamus. Notice the nodule in the left hippocampus.

Autopsy.—A tumor originating from the sella turcica compressed the olfactory nerves, the orbital and cingular gyri, the optic nerves, chiasm and tract and the hypothalamus. The sella turcica was eroded but not invaded by the tumor. The entire ventricular system was dilated. The nerve cells throughout the hypothalamus were diminished in number and showed chromatolysis, severe cell changes and loss of iron pigment.

Comment.—The somnolence in this case was undoubtedly caused by the pathologic changes in the hypothalamus, secondary to compression. Destruction of cerebral cortex may have been a contributing factor, since some of the convolutions, such as the gyrus cingulus, were compressed.

CASE 25.—*Suprasellar meningioma extending into the anterior and middle fossa, probably compressing the hypothalamus. Somnolence and parkinsonism. Increased intracranial tension.*

P. C., a woman aged 49, had a history of increasing frontal and occipital headaches and fainting spells, followed by changes in personality, such as belligerence, irritability and forgetfulness.

Neurologic Examination.—The patient was obese, with a masklike facies and drooling of saliva. She yawned continuously and was drowsy, but could be awakened. The pupils were irregular, the right being larger than the left, and both reacted sluggishly to light. There was bilateral papilledema.

Laboratory Data.—The blood chemistry was normal. Spinal tap disclosed an initial pressure of 280 mm. The fluid was clear and contained 3 cells per cubic millimeter, and the total protein measured 46 mg. per hundred cubic centimeters.

Course.—With dehydration the patient became somewhat more alert. Craniotomy was performed in the right frontal region, and a meningioma was found attached to the right middle meningeal artery, extending along the base in the frontal fossa and the anterior portion of the middle fossa. It compressed the frontal, orbital and cingular convolutions and the floor of the third ventricle.

Comment.—Although the brain was not examined at autopsy, the tumor, which was situated

on the inferior surface of the frontal convolutions and extended into the middle fossa, most likely compressed the basal ganglia and the hypothalamus, thus causing the parkinsonian features and somnolence. The role played by the cortical compression, especially the gyrus cingulus, cannot be ruled out.

GENERAL COMMENT

In a previous communication concerned with a series of pure cortical lesions, we [1] expressed the opinion that some fibers for the control of sleep may originate in the cerebral cortex, especially the hippocampal, angular, frontal, premotor and temporal convolutions. Bard's [2] experiments on sham rage indicated that the hypothalamus is to some degree under the control of the cerebral cortex. Spiegel [3] postulated the existence of a primitive center of consciousness in the thalamus, which transmits impulses to the higher centers of consciousness located in the cerebral cortex. The cortex, in its turn, can also influence the thalamus, either in an excitatory or in an inhibitory manner. Spiegel also expressed the opinion that corticofugal impulses to autonomic structures may be conducted, at least partly, by fibers joining the pyramidal system and partly by extrapyramidal fibers from areas 3, 4, 5 and 6. Lucksch,[4] Marburg [5] and others stated that both the hypothalamus and the neighboring portions of the mesencephalon and thalamus, though each center is concerned with sleep, are subject to the control of the cerebral cortex. Brailovsky [6] expressed the opinion that sleep is governed by a complex corticosubcortical mechanism, starting with cortical inhibition. Salmon [7] stated the belief that three structures—the cortex, the hypothalamus and the hypophysis—are of importance in the regulation of sleep.

Keeser and Keeser,[8] on the basis of their studies on barbiturates, concluded that the diencephalon was the least important center of sleep and the cerebral cortex the most important. Meyer [9] stated the belief that a change in the condition of the entire cerebral cortex, as well as the subcortical region, is involved in the production of sleep. Among observers who have denied the existence of a discrete sleep center are Salkind,[10] Nachmansohn,[11] Altschuler [12] and Spadolini.[13]

On the basis of observations in this series of cases and those of other investigators and of some of the evidence derived from neuroanatomic and neurophysiologic studies, the following afferent and efferent connections concerned with the sleep mechanism can be postulated:

1. The medial forebrain bundle (part of the hippocampohypothalamic tract), running between the ventromedial olfactory correlation areas of the cortex and the preoptic and hypothalamic areas. There is some evidence for the passage of a septohypothalamic tract via this bundle.

2. Corticohypothalamic fibers, via the fornix, arising in the hippocampus and ending in the medial and lateral mamillary nuclei and in the adjacent rostral portion of the tuber cinereum. Papez [14] stated that the fornix is an important link in a circuit controlling the mechanism of emotion.

3. Inferior thalamic peduncle. Fibers connecting the cortex and the hypothalamus via this peduncle probably originate in the frontal, temporal and hippocampal convolutions.

4. Hypothalamocortical fibers. Such connections have not been demonstrated, but their existence is probable.

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5. Marburg, O.: Schlaftheorien und Hirnrindenfunction, Wien. klin. Wchnschr. **39**:1076, 1926.

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7. Salmon, A.: Le rôle de corrélations cortico-diencéphaliques et diencéphalo-hypophysaires dans la régulations de la veille et du sommeil, Presse méd. **45**: 509, 1937.

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12. Altschuler, I. M.: Sleep and Epidemic Encephalitis, J. Neurol. & Psychopath. **9**:222, 1929.

13. Spadolini, N.: Alcune considerazioni sulla fisiologia e fisiopatologia del sonno, Note e riv. di psichiat. **55**:283, 1930.

14. Papez, J. W.: A Proposed Mechanism of Emotion, Arch. Neurol. & Psychiat. **38**:725 (Oct.) 1937.

In 21 of the 25 cases belonging to this group (table), the lesion was neoplastic, with a single tumor in 15 cases and multiplied tumors in 6 cases. Of the entire series of cases of tumor, metastatic neoplasm was present in 5, a suprasellar meningioma in 3 and an adenoma of the pituitary gland in 1. Of the 4 cases in which the lesion was non-neoplastic, a cerebral abscess was present in 1, encephalitis lethargica in 1, diffuse syphilitic disease in 1 and vascular disease in 1. The hypothalamus was compressed and showed pathologic changes in the nerve cells in 16 cases. In 2 cases (5 and 15), the hypothalamus was compressed without changes in the nerve cells. In 4 other cases the hypothalamus was actually invaded, while in 1 case there was partial destruction of the hypothalamus. In about

Summary of Observations in 25 Cases of Disturbances in Sleep with Corticodiencephalic Lesions

Lesion	No. of Cases
Neoplasms	
Single	15
Multiple	6
Abscess of brain	1
Encephalitis lethargica	1
Diffuse syphilis of central nervous system	1
Diffuse vascular lesions	1
Compression of hypothalamus	
With changes in nerve cells	16
Without changes in nerve cells	2
Invasion of hypothalamus	4
Partial destruction of hypothalamus	1
Evidence of increased intracranial pressure	18
Ocular manifestations	4
Disturbances of endocrine glands	3
Myxedema	1
Obesity	1
Deviations in temperature (hypothermia)	4
Insomnia, later followed by somnolence	1

16 cases, in addition to compression or invasion of the hypothalamus, there was compression (cases 7, 12, 14, 15 and 16) or invasion (cases 1, 2, 3, 4, 5, 6, 8, 9, 10, 13 and 17) of the basal ganglia. The possibility that the striohypothalamic pathways played a role in the disturbance of the sleep mechanism in these cases cannot be entirely excluded. In 3 of the cases of neoplasm the tumor was situated in the suprasellar region. These cases were placed in the category of corticodiencephalic lesions because the hypothalamus or its pathways and part of the orbital convolutions and the cingular gyri were compressed or involved.

The interference with the circulation of cerebrospinal fluid, as evidenced by increased intracranial pressure, was greater in this series than in the cases of pure cortical lesions previously reported,[1] being present in 18 cases. The intracranial pressure was normal in 7 cases of the present series (3, 9, 10, 11, 14, 16 and 22). In 4 of these cases (3, 9, 10 and 11) the lesion was non-neoplastic and in 3 (14, 16 and 22) a tumor. The high incidence of increased intracranial pressure in the cases of corticodiencephalic lesions is to be expected, since in most of these cases the neoplasm compressed the ventricular system. It is doubtful whether increased intracranial pressure played a role in the causation of sleep disturbance.

Ocular manifestations, in the form of diplopia, ptosis, weakness of ocular movements and impairment in conjugate deviation, were present in 4 cases (16, 18, 21 and 25). Very slight endocrine disturbances were found in 3 cases (23, 24 and 25), and in these cases the tumors were situated in or in the vicinity of the sella turcica. In 1 of the cases of suprasellar meningioma there was myxedema and in 1 obesity. Slight deviations in temperature from the normal in the form of hypothermia were present in 4 cases (1, 10, 12 and 22). Insomnia, later followed by somnolence, was found in 1 case (21).

Pathologic sleep as the result of neoplasms which arise in the cortex and invade or compress the hypothalamus has been reported on by other authors. The cases of cerebral trauma with hypersomnia, as reported by a number of observers (Zingerle[15]; Urechia and Bumbacescu[16]), may also belong to this category, since simultaneous lesions were probably present in the cortex and hypothalamus. Cases of tumors near the hypothalamus, compressing it or its corticohypothalamic pathways, possibly belong to the same group. Warren and Tilney[17]; Francioni[18]; Souques, Baruk and Bertrand[19]; Francois and Vernier[20]; Bailey[21]; Wodoginskaja,[22]

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and others described somnolence in cases of tumors in the vicinity of and compressing the hypothalamic region.

SUMMARY AND CONCLUSION

In 25 cases of pathologic sleep, there was involvement of the corticodiencephalic structures. The hypothalamus was compressed in 16 cases, and its nerve cells showed pathologic changes in all of these cases. In 4 other cases there was actual invasion of the hypothalamus, while in 1 case there was partial destruction of the hypothalamus. In 2 cases the hypothalamus was compressed without changes in its nerve cells. In 2 other cases there was no compression of the hypothalamus or changes in its nerve cells. In 16 cases, in addition to compression or invasion of the hypothalamus, there was compression or invasion of the basal ganglia with implication of the striohypothalamic pathways. Three cases in which tumors occurred in the suprasellar region were placed in this group because the hypothalamus or its pathways and part of the orbital convolutions and cingular gyri were implicated.

Increased intracranial pressure was present in 18 cases and absent in 7 cases. A high incidence of increased intracranial pressure in this group should be expected, as in most of these cases the neoplasm encroached on the ventricular system.

Ocular manifestations, in the form of diplopia, ptosis, weakness of ocular movements and impairment in conjugate deviation, were present in 4 cases. Slight endocrine disturbances were present in 3 cases, and in these the tumor was situated either within or in the vicinity of the sella turcica. Slight deviations in temperature in the form of hypothermia were present in 4 cases.

From this series of cases of corticodiencephalic lesions, it may be assumed that some fibers for the control of sleep originate in the cortex and reach the hypothalamus via (1) the median forebrain bundle, (2) the fornix and (3) the inferior thalamic peduncle.

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MULTIPLICITY OF REPRESENTATION VERSUS PUNCTATE LOCALIZATION IN THE MOTOR CORTEX

AN EXPERIMENTAL INVESTIGATION

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MINNEAPOLIS

During the course of investigations of cortical motor function under the influence of pain impulses originating in the muscles (Gellhorn and Thompson [1]) and of afferent impulses from the hypothalamus (Murphy and Gellhorn [2]) it was observed that stimulation of a discrete focus with condenser discharges at threshold and suprathreshold intensities led to the production of multiple movements instead of isolated muscular contractions restricted to a small bodily subdivision, which have been described repeatedly. On the basis of these observations, it was decided to reinvestigate the question of multiplicity of motor representation versus punctate localization.[3] Experiments conducted in this study and their interpretation are the subject of the presentation which follows.

A vast and detailed literature concerning motor cortical function has accumulated in the seventy-five years since Fritsch and Hitzig's [4] epoch-making discovery of the electrical excitability of this part of the brain. The communications of Fritsch and Hitzig and of Ferrier [5] about the results of electrical stimulation of motor areas began a train of increasingly painstaking analyses of motor cortical representation, the ultimate goal of which seemed to be definitive assignment of each single muscular effector to a segregated locus in the excitable gray mantle. Physiologic dissection of the motor mosaic may thus be said to have culminated in the studies of Sherrington and Grünbaum [6] on anthropoids and of the Vogts [7] and Hines [8] on monkeys. Garol [9] published similar investigations on the motor cortex of the cat. In the face of such well documented and extensive delimitations of function of the motor cortex, accompanied with carefully drawn pictorial sketches of the results obtained, it would seem, at first thought, somewhat superfluous to add yet another series of observations and maps to the abundant cartography of the motor areas in animals. However, a slight change in method based on a fundamental shift in the point of view made a reinvestigation of the function of the motor cortex imperative.

The spur to further analysis of localization of motor function in the cortex led toward as minute parceling of the cortex into units as possible. This has resulted today in such widespread acceptance of the motor cortex as a repository of the functions of individual muscles and even parts of muscles (Fulton [10]) that it has been likened in operation to the keyboard of a piano (Erickson,[11] Penfield and Boldrey [12]), an opinion

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based not only on the results of animal experimentation but on observations made during stimulation of the human precentral gyrus (Penfield and Boldrey,[12] Foerster [13]).

Pari passu, while discrete and topical functional assignment proceeded apace, abetted by cytoarchitectural expansions, statements found their way into the rapidly accumulating body of knowledge concerning the motor area which expressed a point of view at variance with that of the "punctate" localizers. The supporters of the contrary school of thought—that cortical representation is that of movements, not of muscles, and is several and overlapping rather than single and exclusive—have been found largely in the field of clinical neurology and neurologic surgery (notably Jackson,[14] Horsley [15] and Walshe [16]). This point of view seems to be supported by occasional observations reported in papers the primary aim of which was the foundation and elaboration of the mosaic theory (Beevor and Horsley,[17] Sherrington,[8] Hines,[18] Kennard [19]). That, in addition, the peripheral response to liminal stimulation of the motor cortex (contraction of single muscles or parts of muscles) is far removed from the cortical action underlying voluntary movement goes without saying and is pointed out by even the most firm adherents of the hypothesis of punctate localization (Fulton [10b]).

The important question would seem to be: Should experimental investigation of the function of the motor cortex be confined to the obtaining of the barest discernible muscular responses with the weakest possible electrical currents—"sampling" the cortex, as it were—or should the aim be to evoke, by appropriate stimulation, the full potentialities inherent in the gray matter of the motor area? We believe that the latter point of view is the more defensible, not only because such attempts to reveal cortical functions in their totality would seem to be less artificial and more physiologic, but because it does more to explain clinical observations, particularly those on recovery of function in animals and man after removal of portions or of all of the motor cortex (Horsley,[15] Sherrington and Grünbaum,[6] Foerster,[20] Dusser de Barenne,[21] Hines,[18] Kennard [22] and Bucy [23]).

In keeping with this design the following investigation was undertaken, the aim being to evoke as much as possible rather than as little as possible by stimulation of discrete points on the surface of the motor cortex of animals and then to determine whether or not the results obtained were the expression of purely local activity.

Before methods of investigation and observations are recorded, the most important conditions of our experiments and their limitations should be outlined. First, by "as much as possible" in the preceding paragraph is not meant the production of convulsions. The strength of stimulation, employed in a manner to be described, was purposely suprathreshold in character and ranged from 2.5 to 11 volts. When voltages employed proved to be too high and resulted in convulsions, the corresponding observations were discarded from the series. Next, whereas the recording of combinations of movements was the aim of the experiments, the relationship of these movements to each other in time, so conscientiously recorded by Beevor and Horsley [17] and Hines,[8] was not noted as a rule, for we did not believe such observations to be rele-

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vant to the particular problem under study. Also, in the charting of cortical areas from which movements were obtained, the relative magnitude of such movements from point to point is not indicated in the figures which follow. This, again, appeared to be a side issue. Lastly, the observations were confined to movements of the striated muscles of the face and extremities.

The true purpose, in fine, of this study was to investigate experimentally the principle of the multiple representation of movements in the motor cortex insisted on by Jackson [14] and reiterated by Walshe.[24] We did not, and do not mean to, deny the validity of previous investigations which have had as their intent the revelation of discrete and exclusive muscular foci in the gray mantle. We do mean, however, to shift emphasis from isolated cortical representation to more inclusive cortical function.

The reason for employing members of three animal species (rabbit, cat and monkey) rather than confining attention to the highest of the three was a desire to see whether or not the results obtained under our experimental conditions were correlated with the principle of progressive encephalization (von Monakow,[25] Dusser de Barenne,[21] Fulton,[10b] Sherrington [3]). This was, indeed, found to be the case, but to a lesser degree than expected. The broad principle of multiple representation has been found to be maintained throughout this restricted arc of the phylogenetic hierarchy.

METHODS

Four rabbits, 7 cats and 6 monkeys were employed as experimental animals. The monkeys (Macacus rhesus) were adolescent and in good health, as evidenced by their life in confinement of over one year. An injection of 0.45 cc. per kilogram of body weight of a solution containing 0.1 Gm. dial and 0.4 Gm. ethyl carbamate per cubic centimeter was given intraperitoneally in all species. Inasmuch as the investigations in the monkey were confined to the precentral and postcentral gyri, reported depression of the premotor cortex by this narcotic (Fulton and associates [26]) was not considered important. Administration of ether by inhalation was frequently added during the exposure of the cerebral hemispheres but was discontinued during the period of stimulation.

The head was rigidly held in the frame of the Horsley-Clarke instrument, to which electrode holders provided with rack and pinion were attached. This arrangement, precluding careful observation of movements of the head or neck, did not militate against the original plan of experiment. The body was supported in such a manner that the head was lower than the caudal region, to counteract the known hypotensive effects of dial (Fulton and associates [26]), and that the extremities could move freely.

Unilateral or bilateral craniectomy—the latter in stages—was undertaken by the usual methods, particular attention being paid to careful hemostasis to prevent subarachnoid hemorrhage. In the cat, this meant careful thermocoagulation of fine, almost invisible vessels running from the surface of the cortex to the cerebral dura, the presence of which is not noted in previous descriptions of the intracranial anatomy of this animal. To insure adequate exploration of all of the lateral and under surfaces of the cerebral hemisphere in the cat, the eye was either removed or retracted inferiorly by the placement of sutures in the superior rectus muscle. The latter procedure, while denying as much available area as removal of the eye and orbital tissues, proved much less shocking than the more radical operation. When it was feared that shock had supervened, ephedrine was given and stimulation postponed.

The dura was carefully reflected medially, and vessels entering the superior sagittal sinus were left intact unless their presence interfered too greatly with free exploration, in which case they were coagulated and divided. In instances in which this was necessary adequate drainage of the cortex would seem to have been still maintained.

Such deterrent factors to optimal cortical function as cooling of the brain, drying of the surface and general hypothermia (Sherrington [3] and others) were combated by the placing of lamps, one over the body of the animal and another in close proximity to the exposed hemisphere, and the frequent application of warm Ringer solution to the cortex. Saturated pledgets of cotton were arranged over the area of decompression so as to form a moist chamber. Neither of these procedures resulted in the physical spread of current predicted by other investigators (Garol [9]). As in previous investigations,[27] the cortex was stimulated through bipolar silver electrodes placed 2 to 3 mm. apart with Goodwin's [28] apparatus, which permits independent control of duration, frequency and intensity of condenser discharges.

The frequency of stimuli chosen for almost all stimulations was 90 per second. This is at the upper range of frequencies considered by Hines and Boynton [29] to be most effective during stimulation with sine waves, and in our own hands it has proved to be best suited for the purposes used. Voltages were almost always supraliminal but far below convulsive level. The duration of impulse was 20 milliseconds (Garol [9]); the period of stimulation, ten seconds. Therefore, the conditions were those of primary facili-

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tation (Bubnoff and Heidenhain,[30] Brown[31] and Adrian[32]). One or two minutes was allowed to elapse between successive stimulations. This time was considered long enough to allow after-effects from previous facilitations to be dispersed and to obviate "secondary facilitation" (Brown,[31c] McCulloch[33]), since constancy of cortical response prevailed under these conditions.

In the rabbit, the cortical area stimulated consisted of all that was responsive, beginning anteriorly and moving posteriorly until silent cortex was encountered. This usually proved to be about one-third the distance from the frontal pole to the torcular Herophili. The far posterior, occipital, area found by Exner[34] to be productive of movements of the foreleg was not included. In the cat, the gyri stimulated included the anterior and posterior sigmoid gyri; the coronal gyrus; the gyrus proreus; the gyrus lateralis; the anterior and middle suprasylvian gyri; the anterior, middle and posterior ectosylvian gyri, and the anterior, middle and posterior sylvian gyri (Winkler and Potter[35]). Exploration in the monkey was confined to the precentral and postcentral gyri and therefore encompassed areas 4q and 4r of McCulloch,[33] area 44 and the posteroinferior tail of area 6, as well as areas 3, 1, 2 and 5. Stimulations in the monkeys were arbitrarily discontinued at what was thought by gross inspection to be the posterior limit of the strip, or suppressor area, of Hines.[18] All of areas 4q and 4r may therefore not have been stimulated in certain instances, but inasmuch as the intent of the investigation was to confirm a principle, and not to evoke all movements wherever possible, this was of small moment.

In order to decide the part played by physiologic spread of impulse and that by purely local activity at the point stimulated, certain cortical points were isolated by transcerebral section. Typical examples of such experiments are recorded later. In performing these isolations, the intent was to cut through not only the cortex proper but the U fibers, although evidence concerning physiologic spread in he cortex (Adrian,[32] Erickson,[36] Fulton,[37] McCulloch,[33] Rosenblueth and Cannon[38]) indicates intracortical transmission only under conditions of primary facilitation. Isolation was made on all four sides in some experiments and on only three in others in which the tissue posterior to the block segregated surgically was electrically nonresponsive. The depth of incision was checked at autopsy, after fixation of the brain in solution of formaldehyde U. S. P. (1:4). It was found in almost all cases to have been deep enough to interrupt not only intragriseal but possible U fiber conduction pathways. Sketches of these isolated blocks are presented in figures 6, 7 and 8, with respective protocols described in tables 1, 2 and 3. To mitigate the effect of the factor of trauma, stimulation of the isolated block was not undertaken until an interval of ten to thirty minutes had elapsed.

RESULTS

Figures 1, 2 and 3 present pictorially the results of stimulation under conditions of primary facilitation in individual rabbits, cats and monkeys. Each symbolic line, the significance of which is indicated in the legends, encompasses the area of the excitable cortex which responded to stimulation by a movement through a particular joint to any degree, no discrimination being made with reference to intensities of response.

The principal observation in the investigation which applies to the three species studied may be summarized in the statement that under conditions of primary facilitation, multiple representation of movement is widespread in the motor cortex of the rabbit, cat and monkey. The most common type of multiple representation is that found within large somatotopic divisions (leg, arm, face). As figures 1 to 3 demonstrate, there is considerable overlap of the areas from which movements activating the various joints of the leg or of the arm are elicited, and a similar statement applies to the face and head area. Thus, in figure 2 *A* and *C* show almost complete identity of the boundaries of the cortical areas for movements of the hip, knee and hindfoot in the cat, while in figure 3 *A* and *C* illustrate that in the monkey the cortical areas for movement of the hip, knee, ankle and toes practically coincide, as

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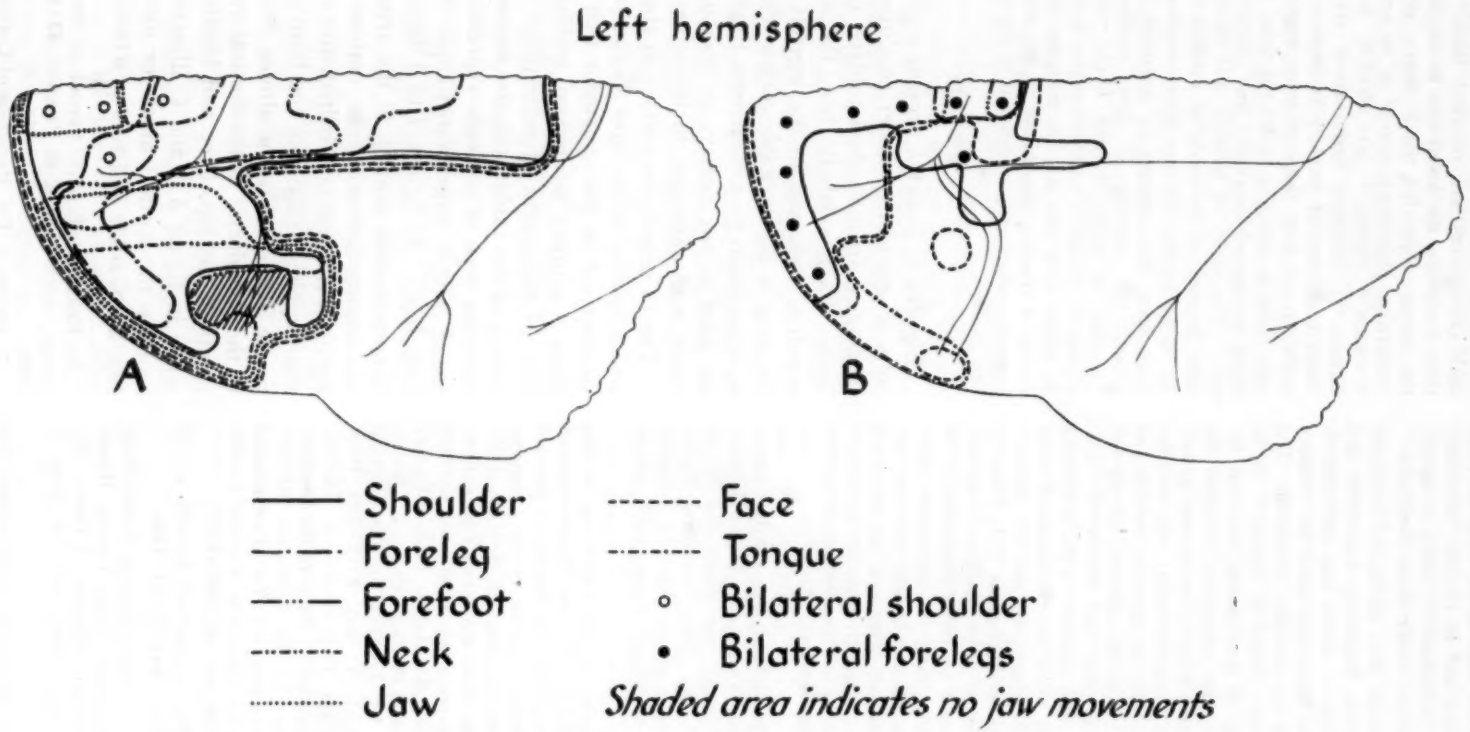

Fig. 1.—Maps of cortical motor response (left hemisphere) in the rabbit (2 animals), summarizing the results of suprathreshold stimulation with condenser discharges under conditions of primary facilitation. Extensive overlap of movements with multiplicity of representation is shown.

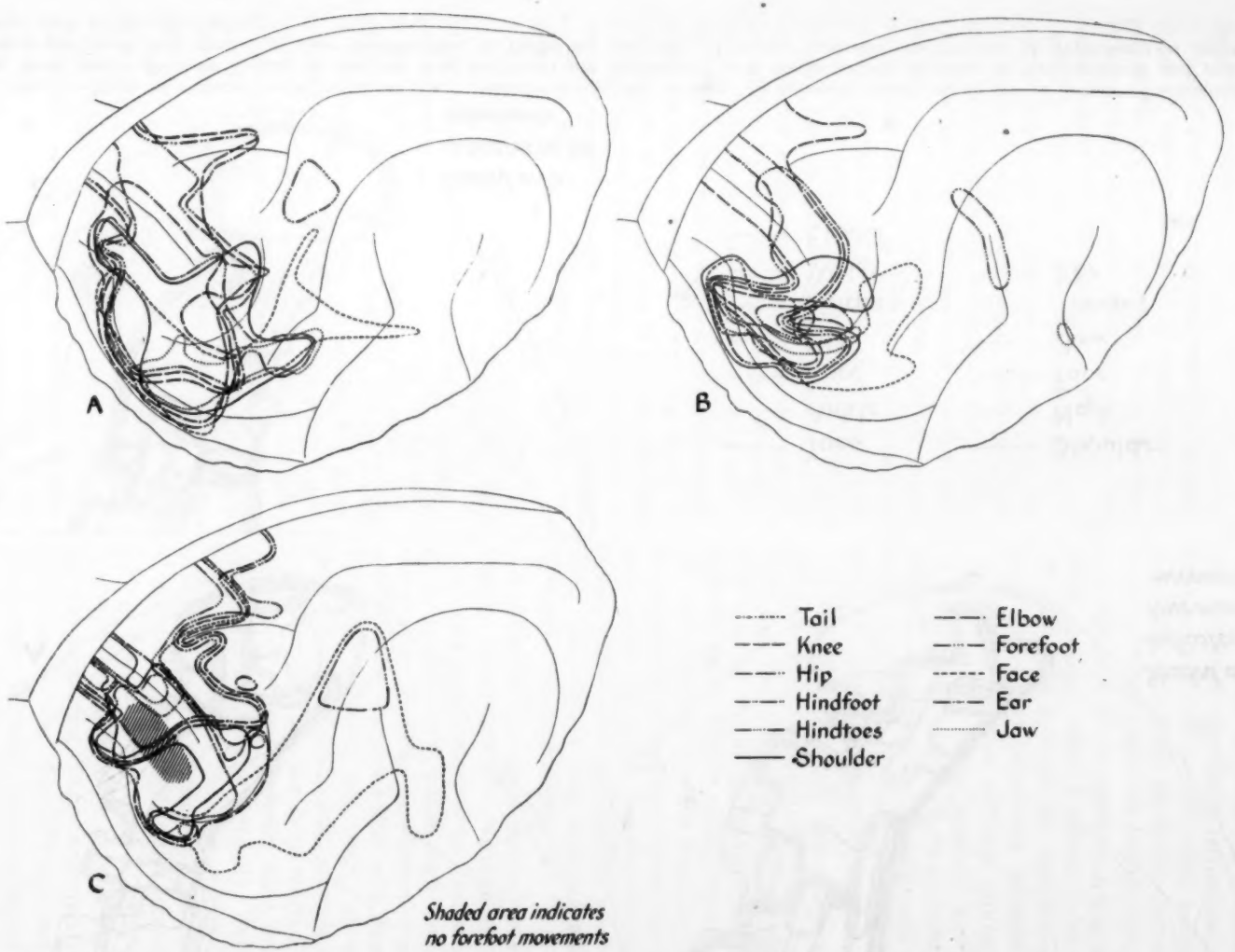

Fig. 2.—Maps of cortical motor response (left hemisphere) in the cat (3 animals) under conditions of stimulation similar to those noted for figure 1. In general movements of the hindleg are medial and posterior, and responses of the foreleg and face, anterolateral and posterolateral, respectively, but widespread multiplicity of representation is clearly evident.

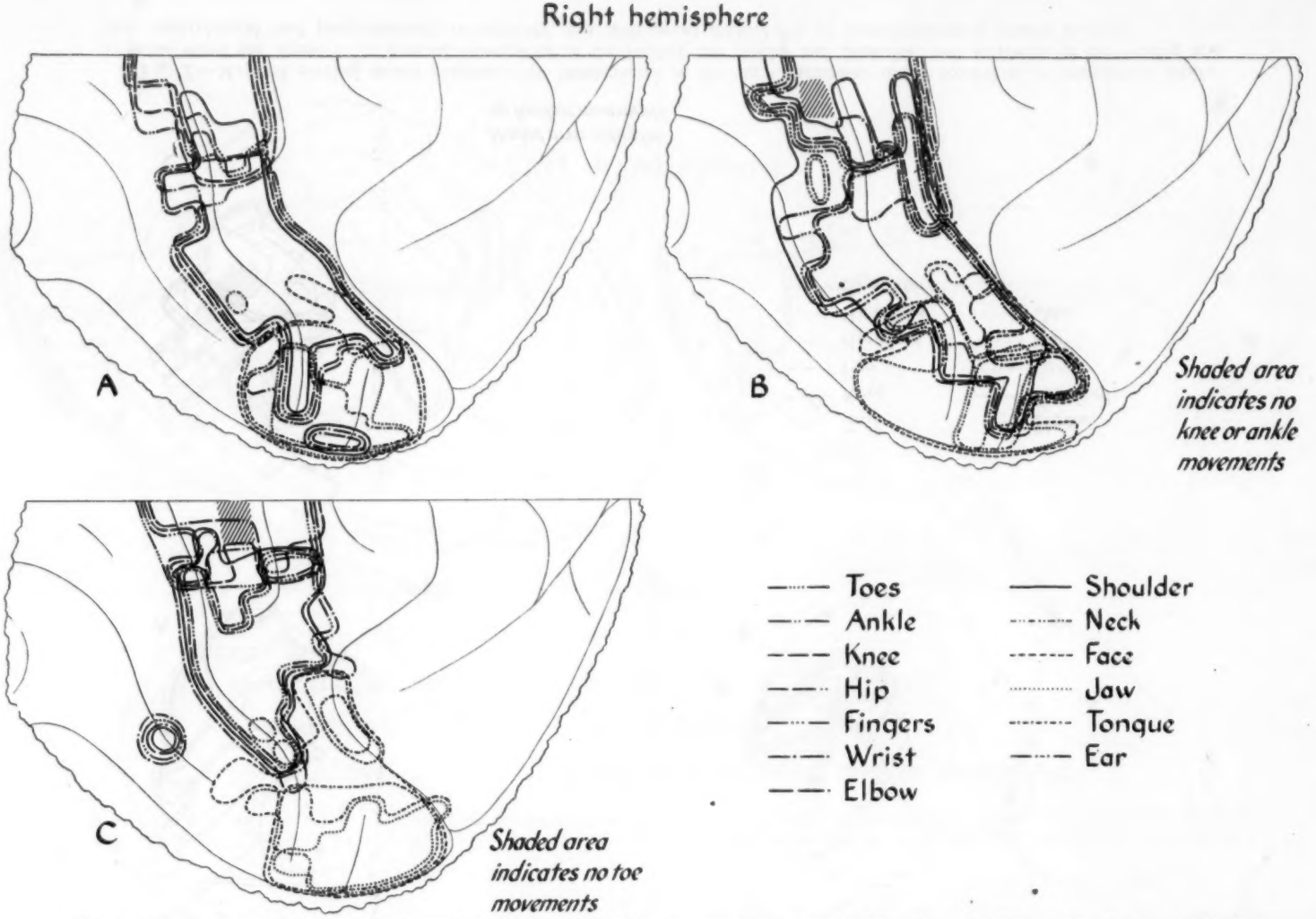

Fig. 3.—Maps of cortical motor response (right hemisphere) in the monkey (3 animals) under conditions of primary facilitation. The three major divisions (areas for the leg, arm and face) are represented in a medial-lateral direction in the precentral and post-central gyri, with less overlap of their borders than in the rabbit and cat. However, extensive multiplicity of representation exists within each of the three areas.

do the boundaries for movements of the shoulder, elbow, wrist and fingers. There is less agreement in the boundaries of cortical areas for the facial muscles, tongue, jaw and ear in the cat and the monkey, although considerable overlap is found here too.

Cortical overlap of two large somatotopic subdivisions, likewise found in all three species, is greatest in the rabbit and least in the monkey. It apparently decreases with progressive encephalization as the phylogenetic scale is ascended. The cortical areas representing movements of the shoulder, face and tongue are almost coextensive in the rabbit (particularly in figure 1 *A*), and considerable overlap of the cortical areas representing movements of the jaw and shoulder also exists. Extensive overlap of the cortical areas for the hindleg and foreleg, as well as those for the foreleg and face, is seen in figure 2 *A* to *C*, but, despite considerable individual differences, there is less overlap of the areas for the face and the foreleg in the cat than was seen in the rabbit. Finally, the large somatotopic divisions coincide least in the monkey (fig. 3 *A* to *C*), but it is worthy of note that the movements activating the various joints of the foreleg could be elicited from a small portion of the area for the hindleg. Such overlap is found more extensively between the face and the foreleg area, although enormous quantitative differences exist in individual animals.

Close inspection of figures 1 to 3 reveals that even in the rabbit there are boundaries beyond which certain movements cannot be obtained despite responsiveness of the gray mantle, and in the monkey these boundaries are more constrictive. In the latter animal the borders more or less correspond to those delimiting the large sensorimotor areas of Dusser de Barenne [39] but are not as sharply exclusive. There is little physiologic correspondence under our experimental conditions to cytoarchitectonic fields (monkey). The maps summarizing these observations in representative examples (figures 1, 2 and 3) are far different from those accepted as indicative of functional localization in the animals investigated.

Inasmuch as punctate or mosaic localization was not our intent, there would be no point in correlating movements represented with individual foci. However, certain features of the results of our stimulations merit individual, but brief description.

1. Most of the experiments, as noted, were conducted with the intensity of stimulation above threshold. Even at threshold, however, and under conditions of primary facilitation, a multiple response was the rule. In only 1 monkey experiment was an isolated muscular contraction, that of the extensor digitorum longus, seen.

2. Although our preoccupation was with movements through joints, a cortical point which, for example, was recorded as representing "wrist" alone was still a point with multiple activities, for wrist movements were not simply flexion or extension; they were "fixation" (cocontraction of extensors and flexors). As might be expected, this was usual when wrist movements were combined with flexion of the fingers, but it was also true when wrist movement was seen alone.

3. Surprisingly—and this is extremely important—the movements most widely represented were not the most peripheral: Following Jackson [14] and Walshe,[24] we had anticipated that the opposite would be true. Such, however, was not the case. As may be seen from a glance at the accompanying maps, movements through proximal joints (shoulder, knee) were at least as widely evoked as were reactions involving more distal joints (paws, fingers, toes), and in some instances even more widely.

4. Although our maps purposely avoid a distinction between the occurrence of a certain movement as a primary or as a secondary movement, several experiments were conducted on cats in order to determine whether or not cortical points which responded first with flexion of the knee, for instance, and, then, as stimulation proceeded, with additional movements had a lower threshold for the knee reaction than had other points from which the knee reaction was obtained secondarily or tertiarily. There was no correlation between the level of threshold for a movement and its primacy of response. Equally of interest is the fact that the accepted "knee" area in the cat, for example (Garol [9]), did not have a lower threshold for knee movements than did more outlying (with reference to Garol's map) regions, and this held true for all other movements. However, a low threshold area was found consistently at the lower, lateral, end of the cruciate sulcus and for about 5 mm. around it in all directions.

5.[40] In many individual stimulations, there was a latency of motor response, referred to in

39. Dusser de Barenne, J. G., and McCulloch, W. S.: Functional Boundaries in the Sensori-Motor Cortex of the Monkey, Proc. Soc. Exper. Biol. & Med. **35**:329-331, 1936. Dusser de Barenne, J. G.: Sensori-Motor Cortex and Optic Thalamus, in Report of Eleventh International Congress of Psychology, Paris, 1937.

40. Paragraphs 5 to 12 refer to incidental observations which seemed worthy of record.

The three major divisions (areas for the leg, arm and face) are represented in a medial-lateral direction in the precentral and postcentral gyri, with less overlap of their borders than in the rabbit and cat. However, extensive multiplicity of representation exists within each of the three areas.

previous communications from this laboratory, of one or more seconds after application of stimulus. This was undoubtedly the expression of "summation time" (Adrian,[32] Cooper and Denny-Brown [41]), and it has been noted to be of similar length—up to 5 or 6 seconds—by others (Clark and Ward [42]). The length of latency in our hands may have been due to the relatively high frequency of stimulation (Rosenblueth and Cannon [38]). It was particularly obvious in the monkey during stimulation of the parietal and precentral operculums.

6. The movements observed evidenced cocontraction, as well as the reciprocal innervation which Sherrington [3] observed during cortical activity. The degree of cocontraction and its timing in the motor response are to be investigated further by electromyographic studies, but its presence was established beyond doubt by observation and palpation of muscles and by preliminary myograms. This is supportive evidence of the relatively physiologic character of these experiments, for, as noted by Jackson [14] and others,[43] coinnervation is the rule in voluntary movement.

7. Although, owing to rigid fixation of the electrodes and suitable intervals of stimulation, the cortical response was quite constant, it was seen that variations in the intensity of stimulation influence the response not only quantitatively but qualitatively. With near threshold stimulation, movements were often extensor in type, particularly in the monkey. With increase in intensity, flexor movements became predominant. Although no further analysis was attempted, it is realized that this result depends not only on the cortex but on the relative strength of flexor and extensor muscles, as well as on the state of the lower motor neuron (Magnus [44]).

8. The movements observed in the monkey were pseudopurposive in character but were also strangely like dystonic contractions characteristic of choreoathetosis in the human being. Bucy [45] has called attention to the similar appearance of movements elicited by stimulation of the premotor cortex of the macaque. We believe that this applies to the motor cortex proper and may be pertinent to the problem of surgical relief of dystonia by excision of the precentral rather than the premotor cortex in man (Horsley,[11] Bucy [23]).

9. Inhibitory, as well as excitatory, responses were noted in all three species from stimulation of foci not known to be suppressor in character. This inhibitory response was effective on spontaneous activity. It was often obtained with lower intensities than were excitatory effects and indicated the approach of the excitatory threshold. In addition, it was frequently observed that

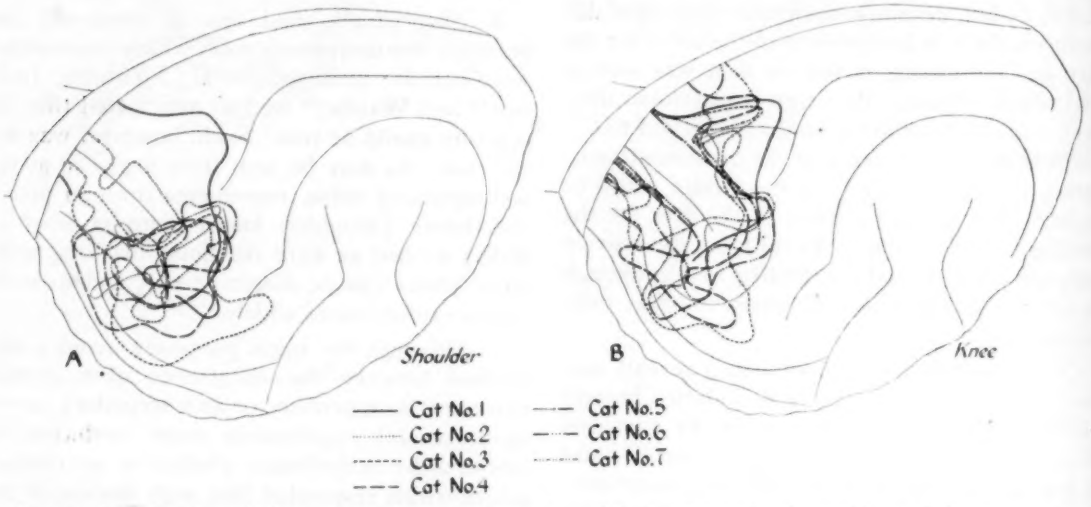

Fig. 4.—Individual variations in cortical representation (left hemisphere) of shoulder and knee movements, respectively, in 7 cats.

41. Cooper, S., and Denny-Brown, D. E.: Responses to Stimulation of the Motor Area of the Cerebral Cortex, Proc. Roy. Soc., London, s. B **102**:222-236, 1927.

42. Clark, S. L., and Ward, J. W.: Electrical Stimulation of the Cortex Cerebri of Cats, Arch. Neurol. & Psychiat. **38**:927-943 (Nov.) 1937.

43. Hathaway, S. R.: An Action Potential Study of Neuromuscular Relations, J. Exper. Psychol. **18**:285-298, 1935.

44. Magnus, R.: Körperstellung, Berlin, Julius Springer, 1924.

45. Bucy, P. C.: The Relation of the Premotor Cortex to Motor Activity, J. Nerv. & Ment. Dis. **79**: 621-630, 1934.

the excitatory effect characteristic of the area stimulated followed the inhibitory action after a latency of one or more seconds.

10. After-discharge was sometimes seen after termination of ten seconds' stimulation in all three species but was not recorded as movement from stimulation. Intensities were usually reduced, and the experiment was repeated. Although not pertaining to our specific problem, it may be mentioned that after-discharge often anticipated the "true" motor response obtained with a slightly higher degree of stimulation. In isolation experiments, section through the anterior lip of the central sulcus did not prevent the appearance of after-discharge. Both of these observations are contrary to the statements of Sapirstein.[46]

11. With suprathreshold but subconvulsive stimuli no movements of the hindlegs or the ear were elicited in the rabbit.

12. "Islands" of limited representation in the midst of fully responsive regions may correspond to the silent zones noted by Sherrington [3] (figs. 1 *A*, 2 *C* and 3 *B* and *C*).

Figures 4 and 5 depict a phenomenon which appears to be the laboratory counterpart of Penfield and Boldrey's [12] observations based on a series of stimulations of human brains. These figures indicate a considerable lack of correspondence from animal to animal of areas responsive with shoulder and knee movements in

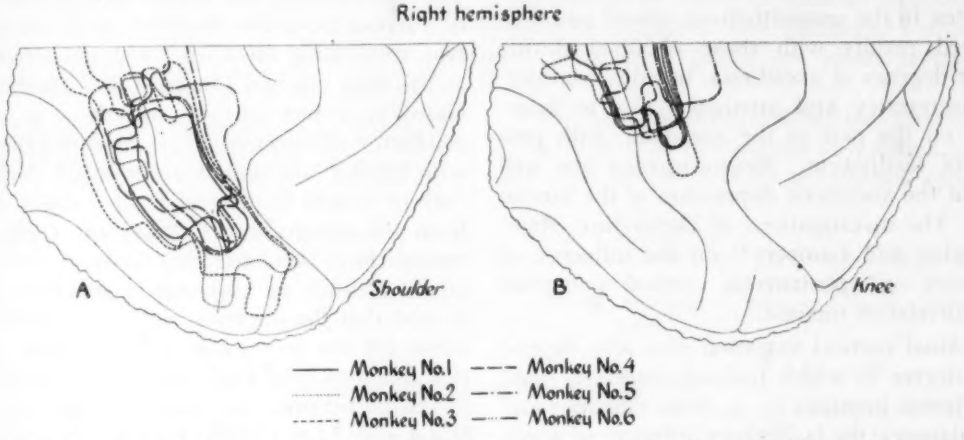

Fig. 5.—Individual variations in cortical representation (right hemisphere) of shoulder and knee movements in 6 monkeys.

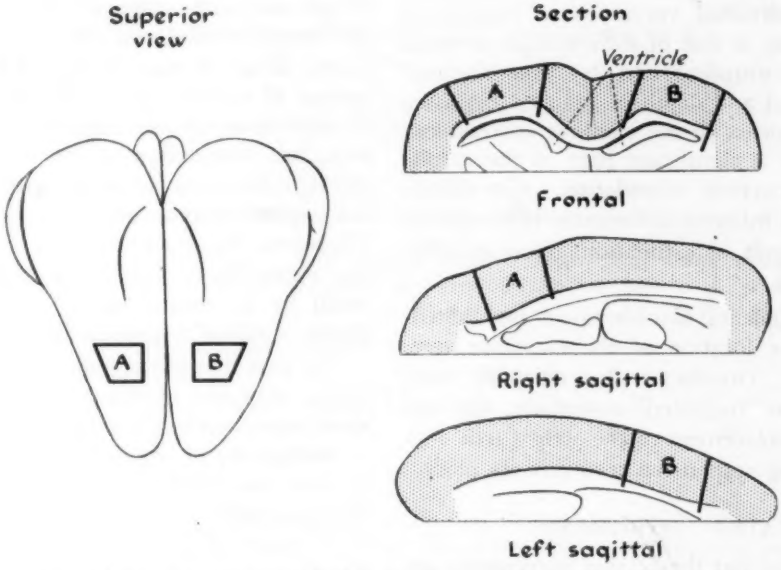

Fig. 6.—Diagrams of isolation of two cortical foci (3 by 5 mm.) in the rabbit. Results of stimulation are recorded in table 1.

46. Sapirstein, M. R.: Characteristics of After-Discharge Following Cortical Stimulation in the Monkey, Arch. Neurol. & Psychiat. **46**:665-675 (Oct.) 1941.

the cat and monkey. Again, individual variation is less extensive in the more "encephalized" monkey but is still present to a measurable degree. Factors to which this discrepancy is accountable are numerous; perhaps most important is the degree of narcotization. Ferrier [5] early recognized the influence of the depth of anesthesia on cortical response, as did Bubnoff and Heidenhain.[30] Clark and Ward,[42] in a remarkable series of experiments on cats, in which they stimulated the cortex in the unanesthetized animal and then compared results with those obtained during varying degrees of anesthesia, noted a considerable discrepancy and attributed this to interference on the part of the anesthetic with processes of facilitation. Neurosurgeons are well aware of the anesthetic depression of the human cortex. The investigations of Derbyshire, Rempel, Forbes and Lambert [47] on the influence of anesthetics on spontaneous cortical potentials are of correlative interest.

Individual cortical variation may also depend on the degree to which narcosis interferes with tonic afferent impulses (e. g., from thalamus and hypothalamus), the facilitatory influence of which has been previously demonstrated.[27]

Another factor to be considered as an explanation of the individual variations in location of responsive areas is that of difference in cerebral topography, emphasized by Sherrington.[3] Breadth of sulci and depth of fissures, exposing more or less cortex to the exciting current, undoubtedly play a significant part in the results obtained by cortical stimulation. Circulatory differences and inherent differences in threshold, extremely difficult of estimation, likewise influence the results.

Also, developmental considerations undoubtedly influence the location of the excitable area. In figure 3*C* (monkey) the excitable area seemed to have "migrated" anteriorly, the end result being displacement of the strip (area 4-s) forward, leaving responsive cortex in its place.

ISOLATION EXPERIMENTS

The validity of our thesis, that movements are represented severally rather than singly in the motor cortex, depends on the success of experiments in which the cortical points stimulated were isolated from the surrounding gray matter. These crucial experiments will be reported in detail.

47. Derbyshire, A. J.; Rempel, B.; Forbes, A., and Lambert, E. F.: The Effects of Anesthetics on Action Potentials in the Cerebral Cortex of the Cat, Am. J. Physiol. **116**:577-596, 1936.

The importance of such cortical isolations to the soundness of our argument was recognized from the start of this investigation, for it is freely admitted that the results depicted in the maps previously referred to might be accountable to (1) physical spread or (2) physiologic spread of the exciting impulse under the conditions of primary facilitation.

Before block segregations of reactive foci were undertaken, the degree of physical spread of current from the electrical field between the two stimulating electrodes was determined. If, as has been claimed (Bubnoff and Heidenhain,[30] Garol [9]), a wet cortical surface is a uniform conductor of electricity in all directions, even with bipolar stimulation, considerable leakage of current should be detectable at a short distance from the electrodes. Cathode ray oscilloscopic records have demonstrated, on the contrary, the falsity of such an assumption and have clearly proved that the electrical field, even with stimulation for ten seconds at relatively high intensities, remains restricted, practically speaking, to the tissue between the electrodes. During stimulation with 11 to 12 volts for the period described (ten seconds) there is a sharp drop in voltage from that found between the electrodes to about 50 per cent of the original value 1 mm. away from the interelectrodal area and to about 25 per cent 2 mm. away. It may be argued that there is still spread of current physically, even though it be of only 50 or 25 per cent of the whole. This is true, but stimulation of the points 1 to 2 mm. distal to the original focus with 50 per cent of the original current caused no response whatever. Therefore, the amount of physical spread under our experimental conditions was negligible and could by no means have accounted for multiplicity of motor response in itself.

The part that physiologic spread of self-propagating neuronal discharges might play is much more important to the solution of the explanation of multiplicity of reaction to cortical stimulation. As first described by Adrian,[32] activation of the deep pyramidal layers in the motor cortex results in a "wave of positivity" which spreads in all directions to points as far as 5 to 8 mm. distant (rabbit). This type of transmission has been seen by Dusser de Barenne and collaborators (McCulloch [33]) during local strychninization of the cortex and is thought to account for the response of broad regions of the cortex to the application of the drug. It is also implicated (Erickson,[36] Rosenblueth and Cannon [38]) in the general epileptic discharge. Therefore, might not physiologic spread under these circumstances account for our results?

It was at this point that cortical isolations were undertaken. Inasmuch as Adrian's "wave of positivity" is believed (Dusser de Barenne and McCulloch [39]) to depend on neuronal synapses within the deep layers (large and giant pyramidal cell laminas), simple incision through the gray mantle on all four sides surrounding a cortical focus should be sufficient to eliminate it. However, because it was felt that intergyral U fiber connections (Mettler [48]) might conceivably conduct some sort of propagated impulse, the depth of incision was calculated to extend through the U fiber layer, at the junction between cortex and subcortex.

Segregations of foci were therefore made in animals from each species. Rectangular cortical islands, measuring 5 mm. long by 3 mm. broad, were isolated. The site of the blocks prepared and their gross appearance in two planes at autopsy are shown in figures 6, 7 and 8. Protocols illustrating the retention of multiplicity of response and its intensification by hypothalamic facilitation (Murphy and Gellhorn [2]) after isolation of cortical points are given in tables 1, 2 and 3.

These tables demonstrate beyond question that representation of movements in a single cortical focus does not depend on physiologic spread of generated neuronal impulses into adjacent areas of the cortex but is a function of the "point" directly stimulated.

It might be pointed out that after cortical isolation stronger stimulation was necessary to evoke the control response, or something very close to it, and even that in 1 experiment tabulated (table 2 *C*) the island reacted only with a "trace" response through one joint. However, hypothalamic facilitation now brought out movements of the shoulder and foreleg which had been present before. It should be added that these were true cortical movements and not due to

TABLE 1.—*Cortical Isolations in the Rabbit (fig. 6)* *

	Intensity (Volts)	Face	Tongue	Jaw	Right Shoulder	Left Shoulder
A. Isolation of Right Frontal Block on Four Sides						
Control	11	+	+	..	+	+
Postisolation	11	..	+	..	..	+
Postisolation	17	++	++	..	++	++
B. Isolation of Left Frontal Block on Four Sides						
Control	11	+	+	..	(+)	++
Postisolation	11	+	++	++	(+)	++

* In this table, and in tables 2 and 3, the scale of gradation of movements is as follows: (+), trace; +, minimal flexion; ++, moderate flexion; +++, maximal flexion. All stimulations were made for ten seconds at a frequency of 90 per second.

TABLE 2.—*Cortical Isolations in the Cat (fig. 7)*

	Intensity (Volts)	Shoulder	Elbow	Forefoot	Hip	Knee	Hindfoot
A. Isolation of Right Frontal Block on Four Sides							
Control	6.7	....	....	....	....	+	+
Postisolation	5.7	....	....	....	....	+	+
B. Isolation of Right Frontal Block on Three Sides							
Control	6.7	(+)	....	....	+++	+++	+++
Postisolation	11	(+)	....	....	++	++	++
Postisolation, hypothalamic facilitation *	11	+	++	....	+++	+++	+++
C. Isolation of Left Frontal Block on Three Sides							
Control	8.2	++	++	++	....	++	++
Postisolation	11	....	(+)	....	....	....	....
Postisolation, hypothalamic facilitation *	11	+	++	....	....	....	....
D. Isolation of Right Frontal Block on Three Sides (between lines 3 and 4)							
Control	9.75	....	....	....	....	++	++
Postisolation	8.25	....	....	....	....	(+)	(+)
Postisolation, hypothalamic facilitation *	8.25	....	....	....	....	+	+

* Simultaneous stimulation of cortex and hypothalamus (mamillary nuclei, inductorium 8 C.D.).

TABLE 3.—*Cortical Isolations in the Monkey (fig. 8)*

	Intensity (Volts)	Face	Jaw	Neck	Shoulder	Elbow	Wrist	Hip	Knee	Fingers	After-Discharge
A. Isolation of Block at Midpoint of Precentral Gyrus on Four Sides											
Control	9.7	....	....	....	+	+	++	....	++	+++	30 sec.
Postisolation	11	....	....	....	+	+	+++	(+)	++	+++	32 sec.
B. Isolation of Block Below Midpoint of Precentral Gyrus on Four Sides											
Control	8.25	....	....	....	++	++	++	....	....	+++	
Postisolation	11	....	....	....	(+)	(+)	+	....	....	++	
C. Isolation of Block at Foot of Precentral Gyrus on Four Sides											
Control	8.25	++	(+)	....	(+)	++	+++	....	....	+++	
Postisolation	11	+++	+	+	....	....	....	....	....	....	

48. Mettler, F. A.: Corticofugal Fiber Connections of the Cortex of Macaca Mulatta: The Frontal Region, J. Comp. Neurol. **61**:509-542, 1935.

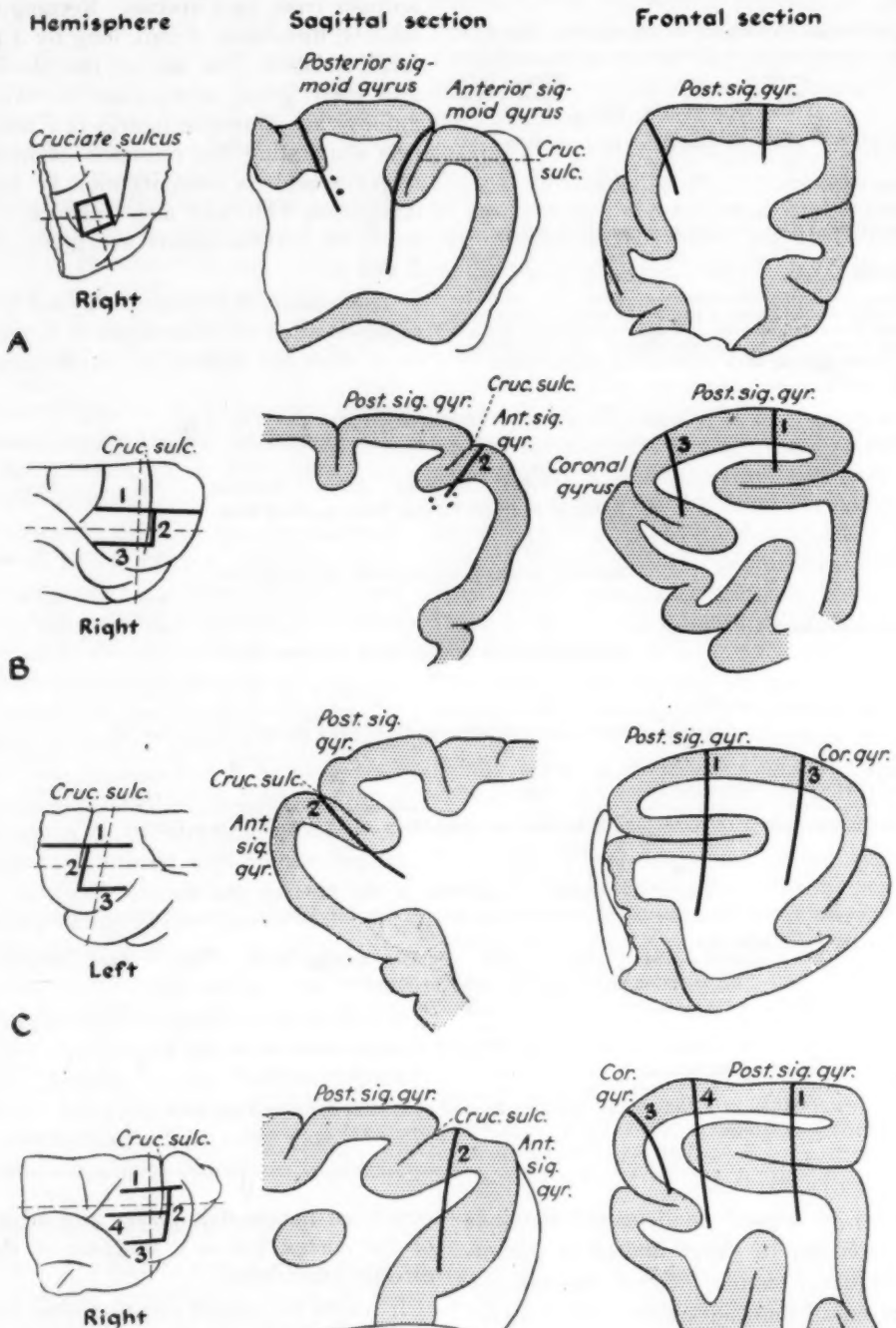

Fig. 7.—Diagrams of isolation of cortical foci (3 by 5 mm.) in 4 cats. Results of stimulation are recorded in table 2. Broken lines through hemispheres correspond to planes of section at autopsy (in *D* the block stimulated is bounded by lines *2*, *3* and *4*).

activation of the hypothalamus as such (Murphy and Gellhorn [2]).

In some experiments not all the movements were retained after isolation, and in many the movements, while still present, were not as strong as in the control. It is believed that these effects are due to trauma consequent on the surgical procedure because in other experiments listed the postisolation reaction was the counterpart of the control and because the islands prepared were very small (5 mm. long by 3 mm. wide). The deep incisions pictured in figure 6, 7 and 8 necessarily interfered with local blood supply, and there was almost invariably some blood in the subarachnoid space overlying the block stimulated.

Even in the face of such traumatic factors, however, and even though some movements formerly obtained were absent after isolation, multiplicity of representation persisted to an often startling degree (strong movements of both extremities). Furthermore, as in the experience of Dusser de Barenne and Marshall,[49] sometimes the strength of movements was intensified after segregation (experiment *B* in table 1).

49. Dusser de Barenne, J. G., and Marshall, C.: On a Release-Phenomenon in Electrical Stimulation of the "Motor" Cerebral Cortex, Science **73**:213-214, 1931.

COMMENT

It was one of our purposes in planning the investigation to devise a type of stimulation which would be as nearly physiologic as possible. Investigators who have used brief-acting, threshold currents, usually faradic in type, admit that the situation is highly unphysiologic and the results observed artificial in the sense that they do not resemble voluntary motion at all (Brown [31d] and Kennard [19]). On the other hand, it would seem logical to suppose that volitional initiation of motor activity, a process of some temporal magnitude, involves the setting up of facilitatory states in the brain, as suggested by Brown. It therefore appears to be more reasonable, in studying the function of the motor cortex, to record and chart its activity under conditions approaching natural stimulation than to restrict the investigation to the effect of brief threshold stimuli, which are probably never operative physiologically.

We conclude, then, that under the influence of facilitatory stimulation, which, although artificial, is of the same order as volitional control, the motor cortex does not consist of a great number of mutually exclusive and independently operative "tiles" of gray matter, the whole forming a mosaic of individual muscular repre-

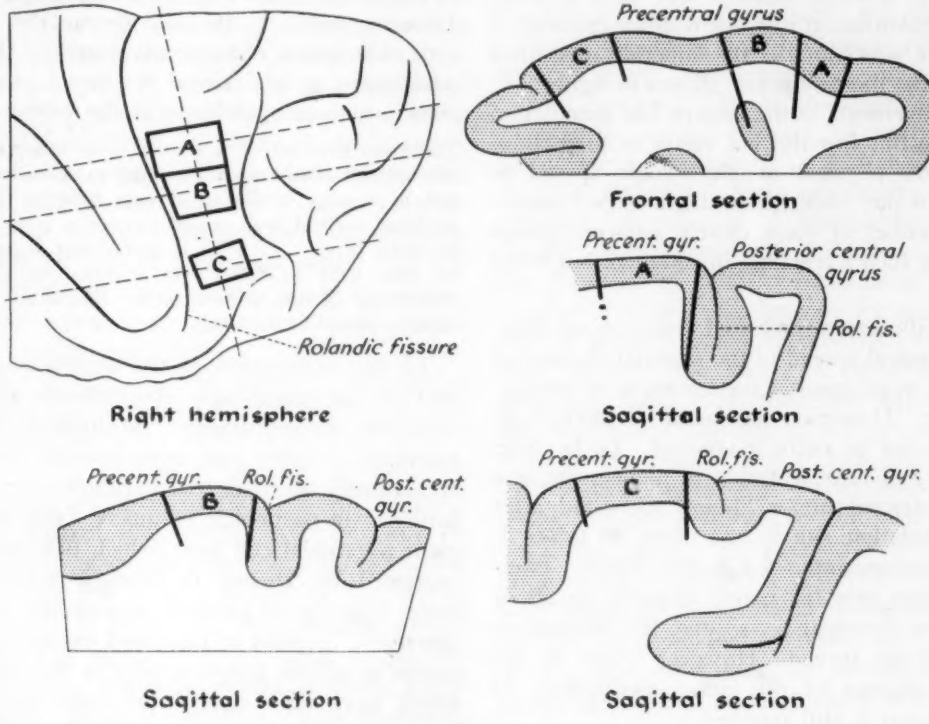

Fig. 8.—Diagrams of isolation of three cortical foci (3 by 5 mm.) in 2 monkeys projected on one diagram. Results of stimulation are recorded in table 3.

sentation, but is, rather, a multipotential organ in which movements of different parts of the somatic musculature are broadly, although not coextensively, represented. The cortex of the brain is a tissue physiologic assay of any single part of which will reveal multipotentiality, but to a degree varying according to the part selected for examination and dependent on the species chosen.

We should reemphasize that these broad and overlapping areas of representation of movements through joints, for example, do have their limitations and that this limitation becomes the more restricted the higher one ascends in the animal hierarchy. A single instance will serve as illustration: Stimulation just below a line connecting the dimple which marks the superior precentral sulcus in the monkey brain, shown in figure 3 *C*, evoked movements of the fingers, but stimulation just above this line did not result in finger motion. Were physical or physiologic spread to account for our results, one might expect stimulation at either of these closely adjacent points to produce such a response in common, but it did not do so.

The oscilloscopic tests cited demonstrate clearly that physical spread of the stimulating current under our experimental conditions is of negligible import. However, the factor of physiologic spread cannot be entirely ignored. To be sure, multiplicity of representation of movements at a single, restricted motor "point" persisted after surgical isolation, but it was often, as tables 1, 2 and 3 demonstrate, of a lesser degree. Traumatic factors may, as noted, account for all or part of this discrepancy; so may the elimination of physiologic spread. However, even in the complete absence of the latter, multiplicity of representation is still retained.

The chief basis of our thesis rests on the isolation experiments. The tissue cut around was just large enough to accommodate the electrodes, which were close together. The incisions went deep enough into the brain to include the intergyral U fibers. In the intact brain stimulation of the cortex under conditions of primary facilitation or excitation of the cortex through volition may involve physiologic spread and, secondarily, spatial facilitation (secondary facilitation of the two forms described by Brown [31c] and Dusser de Barenne and McCulloch [39]). Since the circumsection of a small cortical area rules out physiologic spread, and thereby secondary facilitation of cortical foci not directly stimulated, it is imperative to conclude that multiple representation resides in areas at least as small as those which were isolated in our experiments. It is of interest to point out that the isolated area resembles the intact cortex not only by its retention of muliple representation but by hypothalamocortical facilitation. The effect of the latter on an isolated cortical "point" suggests that some of the loss of representation following isolation was due to trauma, which this powerful facilitatory impulse apparently partially overcame.

The anatomic basis for the extensive functional overlap described in this paper is not likely to be found in the classic cytoarchiteconic maps of the Vogts [7] and their suggested expansion by Lorento de Nó.[50] It may lie in the laminar type of anatomic research advocated by Walshe,[16] who stated in his critical review of physiologic structural correspondence in the motor cortex:

> The areas depicted on a cortical map attempt to take into account all the six component layers of the cortex, and, as it were, strike an average between them: but an ideal cortical map would require a separate sheet for each layer . . . . It seems that in the future we may have to direct our attention to a laminar physiology of the cortex rather than — as we have hitherto done—to an areal.

To this conception of the anatomic counterpart of our physiologic observations we would subscribe wholeheartedly. Multiplicity of representation under our experimental conditions undoubtedly depends on variations in cortical laminas—in particular, lamina V (the large and giant pyramidal cell layer which has been demonstrated by Dusser de Barenne and collaborators [51] to be of greatest importance in motor function). Instead of close and exclusive aggregation of all the ganglion cells in the fifth layer which have their axonal terminus on anterior horn cells going to the biceps muscle of the monkey, for example, these ganglion cells for the biceps are probably distributed, in the fifth lamina, over a very wide range of cortex. Where they are most numerous and closely arranged, stimulation may evoke a contraction of the biceps as a threshold movement or as a prime mover in a series of movements or as the movement which is of greatest magnitude in the complex. How-

50. Lorente de Nó, R.: The Cerebral Cortex: Architecture, Intracortical Connections, and Motor Projections, in Fulton,[10b] chap. 15.

51. Dusser de Barenne, J. G.: The Disturbances After Laminar Thermacoagulation of the Motor Cerebral Cortex, Brain **57**:517-526, 1934. Dusser de Barenne, J. G., and Murphy, J. P.: Thermacoagulation of Motor Cortex Exclusive of Its Sixth Layer, J. Neurophysiol. **4**::147-152, 1941.

ever, wherever there are enough of them together to produce, by combined action, any discernible contraction in the muscle innervated, facilitatory stimulation will reveal their presence. Although the cortical maps presented were drawn without reference to intensity of stimulation and magnitude of the response, differences in reaction were observed, and these differences seem best accounted for by the assumption that the specific ganglion cells responsible for a given movement are inequally distributed and of variable threshold excitability.

It should be restated here that, although we have focused our attention in this investigation on the revelation of multiplicity of representation in the motor cortex, observations leading to this conclusion have been repeatedly made since the inception of study of motor cortical physiology. Ferrier [5] early noted that "the areas [of discrete representation] have no line of demarcation from each other, and where they adjoin stimulation is apt to produce a conjoint effect peculiar to each. . . . A slight stimulus of short duration causes only a part of a complex action which is manifested in its completeness when the stimulus is of somewhat greater intensity and duration." Beevor and Horsley,[17] likewise, called attention to the lack of absolute boundaries between areas of localization and observed that "each movement had a center of maximum representation, this gradually shading off into the surrounding cortex." In recent times, Hines [18] reached similar conclusions from her experiments on the macaque, although still contending that the muscle is the final unit of representation, and Dusser de Barenne [21] emphatically denied the reality of mosaic representation in physiologic activity of the motor cortex. Finally, Clark and Ward,[42] in experiments conducted on lightly anesthetized cats, found simultaneous contractions of muscle groups in the contralateral forelimb and hindlimb, just as we did, but left the pursuance of the extent of such overlap to future investigation.

Hughlings Jackson's [14] insistence on the principle of multiple representation, lost sight of until restated by Walshe,[24] is preeminent in all of his discussions of the physiology of the motor areas in man. Horsley,[15] shortly after the turn of the last century, saw fit to make his position clear on this point:

> It should not, in my opinion, be assumed that the effect of a minimal stimulus, evoking, as it often does, but a single movement of one segment of a limb, is a criterion of all that is represented—that is, in that portion of the cortex cerebri. The response elicited from the cortex cerebri by a stimulus is within limits proportional (1) to the strength of the stimulus, and (2) to the degree to which the movements of any given segment or part of the body are represented at the point stimulated. Consequently, a minimal stimulus may only be adequate for one item of several represented at the point stimulated.

A specific and practical application of this principle may be made to a solution of the problem of the causes for return of function in a part of the body—the arm, for instance—when the primary cortical area controlling the movements of this part has been removed or irreparably damaged in toto. Jackson [24] stated the belief that such recovery took place because "the neighboring parts represent the very same region," but others since his time have attributed reparation to "reorganization" of cortical activity (Kennard [22a,b]), to ipsilateral innervation (Fulton [52]) or to activity of extrapyramidal motor areas (Foerster [20]). Although reorganization within motor areas, particularly under the influence of training (Trendelenburg [53]) and during the developmental period, is not denied, the substrate of this "reorganization" must be present. No one would argue for a transmutation of sensory ganglion cells into motor neurons or for a new formation of neurons under any conditions. It is therefore significant that the increased excitability of neurons in adjacent areas after areas 4 and 6 had been removed (Kennard) was revealed by methods of stimulation apparently similar to our own (i. e., primary facilitation). As previously demonstrated, under such stimulatory conditions these areas were found to be excitable in animals without cortical ablations, and therefore the assumption of a radical reorganization would seem to be unnecessary. The evidence cited in favor of the thesis that recovery of motor power is due to activity of the cortex ipsilateral with the lesion is unsatisfactory, since Bucy [54] showed that ipsilateral movements are represented in area 6 and are characterized by gross postural effects ("sustained extension of all joints"), in contradistinction to the specialized movements elicitable from area 4. In addition, Bucy's [23] recent study of

52. Fulton, J. F.: Bilateral Representation of the Lower Extremity in the Motor Cortex of the Chimpanzee, Am. J. Physiol. **101**:36, 1932; footnote 10 *b*.

53. Trendelenburg, W.: Untersuchungen über den Ausgleich der Bewegungsstörungen nach Rindenausschaltungen am Affengrosshirn, Ztschr. f. Biol. **65**: 103-140, 1915.

54. Bucy, P. C.: Ipsilateral Representation in the Motor and Premotor Cortex of Monkey's Brain, Brain **56**:318-342, 1933.

removal of the precentral gyrus in man leads to the conclusion that recovery of function of paralyzed extremities must be due to activity of the part of the precentral cortex remaining—and not to ipsilateral innervation (which has never been recorded for the arm, for example, in man) or to the activity of subcortical mechanism. His experiences are similar to those of Kennard,[22a] who observed greater and more enduring paralysis in contralateral single extremities in monkeys when the whole of the precentral gyrus was excised than when arm or leg areas alone were removed.

Our contention is this: If all cortex responsive in terms of leg movement under conditions of primary cortical facilitation were removed, there would be enduring paralysis of the contralateral leg, with little or no functional recovery. We agree with Jackson, Walshe and Bucy that recovery after removal of all of what is decided to be the leg area during the usual type of briefly acting, liminal, "sampling" stimulation is due to the retention of cortex controlling movements of the leg. That such complete removals would be contraindicated in the surgical treatment of choreoathetosis, when more restricted ablations suffice, is of course obvious.

There is no better way to conclude than to return to first sources and cite the words of Hughlings Jackson[14] as he summed up his beliefs concerning motor representation in the brain:

> Then it may be said that one convolution will represent only the movements of the arm, another only those of speech, another only those of leg, and so on. The facts . . . . show that this is not the plan of structure of the nervous system. Thus, to take an illustration, the external parts x, y, and z are each represented by units of the corpus striatum. But the plan of representation is not that some units contain x largely only, as x_3, others y largely only, as y_3, but that *each* unit contains x, y, and z—some, let us say, as x_3, y_3, z, others as x_2, y_2, z, etc. When we come to the still higher evolution of the cerebrum, we can easily understand that, if the same plan be carried out, a square inch of convolution may be *wanting*, without palsy of the face, arm, and leg, as x, y, and z are represented in other convolutions; and we can also easily understand that *discharge* of a square inch of convolution must put in excessive movement the *whole* region, for it contains processes representing x, y, and z, with grey matter in exact proportion to the degree of complexity.

From this we might today delete "corpus striatum" and substitute "internal capsule," but in essence this prescient quotation (1870) sums up and states our case exactly.

SUMMARY

Under conditions of suprathreshold stimulation (condenser discharges, 90 per second; stimulatory period, ten seconds) involving primary facilitation, multiplicity of representation of movements is found throughout the excitable motor cortex in three species (rabbit, cat, monkey). It is shown that the boundaries within which movements of the various joints of the arm or of the leg are elicited are practically coextensive, and a similar statement applies to the movements of the face and head. The cortical overlap is not restricted to movements represented in each of the large somatotopic areas (leg, arm, face) but transcends them. Thus, foci activating simultaneously or successively movements of the arm and leg and others calling forth contractions of muscles in the forearm and face are found. The overlap of large somatotopic areas seems to decrease with progressive encephalization, but even in the monkey the cortical map obtained under conditions of primary facilitation is far different from the accepted mosaic of representation.

Multiplicity of representation persists after isolation of a cortical focus stimulated and therefore does not depend on physiologic spread of initiated intracortical waves of impulse, nor is it due to simple physical spread of current. It is, therefore, an inherent property of the motor cortical gray matter and discretely resident within it. Movements, not muscles, are much more widely represented than the usual localization maps, obtained by threshold stimulation with briefly acting electrical currents, indicate. There are, however, boundaries within the excitable area beyond which a given movement cannot be evoked.

The anatomic substrate of the observation of multiplicity of representation in the motor cortex is thought to consist of local variations in population density of specific ganglion cells in the fifth cortical lamina. Consequently, neurons controlling certain movements are not confined to small cortical areas composing a mosaic of sharply delimited units but are interdistributed throughout relatively broad zones. Where a reaction is obtained as a prime movement, there ganglion cells distributed to the spinal segments involved are probably found in heaviest concentration and possess the lowest threshold. But the other members of a series of movements also have their local representatives, which are called into action particularly with higher intensities of stimulation. Without primary facilitation, however, excitable

foci are present only where the density of population of specific neurons is greatest and their threshold lowest. Under these conditions the well known cortical mosaic results.

Contrary to expectations, movements involving distal joints are not more widely distributed than are movements involving proximal joints. Similarly, the threshold for a given movement under conditions of primary facilitation was not necessarily lower in a cortical area where it appeared first in a sequence than in other foci where it developed as a secondary or tertiary movement.

Multiplicity of representation and extent of representation of movements far beyond the bounds delimited by threshold stimulation undoubtedly account for recovery of function of individual parts of the body after the contralateral controlling cortical area has supposedly been removed in entirety.

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DISSEMINATED OLIGODENDROGLIOMA

C. M. BLUMENFELD, M.D., AND W. JAMES GARDNER, M.D.

CLEVELAND

Oligodendroglia was defined by del Río Hortega [1] in 1921. Three years later, Bailey and Hiller [2] suggested that certain gliomas were composed of oligodendrocytes. In 1926, Bailey and Cushing [3] set apart a group of brain tumors as oligodendrogliomas; this publication was soon followed by several reports of similar tumors (Dickson,[4] Schaffer [5] and Thomas and Jumentié [6]). That such tumors were composed of cells which were impregnated like normal oligodendrocytes by del Río Hortega's method was shown first by Bailey and Bucy.[7] Thus, oligodendroglioma was established as an entity. The average incidence of oligodendroglioma in the cases of glioma reported by Bailey [8]; Baker [9]; Elvidge, Penfield and Cone [10]; Gagel [11]; Környey,[12] and Löwenberg and Waggoner [13] was 3.4 per cent (74 of 2,131), ranging from 1.3 per cent of Gagel's series to 8.4 per cent of Környey's cases. From the beginning, it has been considered a glioma with a relatively good prognosis, an opinion based on frequent reports of a long antecedent history, long postoperative survival, a narrow zone of transition from tumor to uninvolved brain, few or no mitotic figures and calcification. As a result, observations which indicate that the oligodendroglioma is second only to the medulloblastoma in its propensity to become disseminated through the ventricles and the subarachnoid spaces have been neglected. The case reported here presented a diagnostic problem for fourteen years. It is an instance of disseminated oliogodendroglioma. The knowledge that this tumor may spread into the subarachnoid space might have led to an earlier diagnosis in this case and may prove helpful in the future.

From the Cleveland Clinic and the Institute of Pathology, Western Reserve University.

1. del Río Hortega, P.: Estudios sobre la neuroglia: La glia de escasas radiaciones (oligodendroglia), Arch. de neurobiol. **2**:16, 1921.

2. Bailey, P., and Hiller, G.: The Interstitial Tissues of the Central Nervous System: A Review, J. Nerv. & Ment. Dis. **59**:337-361, 1924.

3. Bailey, P., and Cushing, H.: A Classification of the Tumors of the Glioma Group on a Histogenetic Basis with a Correlated Study of Prognosis, Philadelphia, J. B. Lippincott Company, 1926.

4. Dickson, W. E. C.: Oligodendroglioma of Floor of Third Ventricle, Brain **49**:578-580, 1926.

5. Schaffer, K.: Bemerkungen zur Histopathologie des Hirngliome, Monatschr. f. Psychiat. u. Neurol. **65**:208-229, 1927.

6. Thomas, A., and Jumentié, J.: Un cas de tumeur du ventricule latéral, Rev. neurol. **2**:202-206, 1928.

7. Bailey, P., and Bucy, P. C.: Oligodendrogliomas of the Brain, J. Path. & Bact. **32**:735-751, 1929.

8. Bailey, P.: A Review of Modern Conceptions of the Structure and Classification of Tumors Derived from Medullary Epithelium, J. belge de neurol. et de psychiat. **38**:759-782, 1938.

9. Baker, A. B.: Intracranial Tumors, Minnesota Med. **23**:696-703, 1940.

10. Elvidge, A.; Penfield, W., and Cone, W.: The Gliomas of the Central Nervous System, A. Research Nerv. & Ment. Dis., Proc. (1935) **16**:107-181, 1937.

11. Gagel, O.: Ueber Hirngeschwülste, Ztschr. f. d. ges. Neurol. u. Psychiat. **161**:69-113, 1938.

12. Környey, S., cited by Löwenberg and Waggoner.[13]

13. Löwenberg, K., and Waggoner, R. W.: Gross Pathology of the Oligodendrogliomas, Arch. Neurol. & Psychiat. **42**:842-861 (Nov.) 1939.

REPORT OF A CASE

The patient, a white man, had been struck by an automobile and sustained a fracture of the left parieto-occipital portion of the skull at the age of 10 years. Thereafter he had occasional headaches, which gradually increased in frequency to two or three a week at the age of 17; he was first seen for this complaint on Oct. 23, 1930. During the preceding month he had had "spells," lasting less than one minute, when he could not express himself. He was small, slender and well nourished. The pubic hair was scant and feminine in distribution. His voice was high pitched. There was slight contraction of the inferior temporal portion of both visual fields. A roentgenogram showed an enlarged sella and erosion of the posterior clinoid processes. Numerous additional special studies yielded no significant information. It was considered that he might have a tumor of the pituitary or hypopituitarism due to some other cause. Medical treatment was without avail. Because of persistence of headaches and increase in number of "spells," an encephalogram was made; this showed greatly dilated lateral ventricles and a slightly dilated third ventricle. At craniotomy a gray membrane resembling thickened arachnoid bulged out between the optic chiasm and the optic tracts, puncture of which released colorless fluid.

The anatomic diagnosis of a portion of the membrane was fibrosis of the pia-arachnoid.

The patient's course continued about the same for seven years with respect to the headaches and "spells"; but his general health improved, his voice deepened, he shaved more often and he was able to perform work requiring long application and mechanical skill. A roentgenogram of the skull made in December 1937,

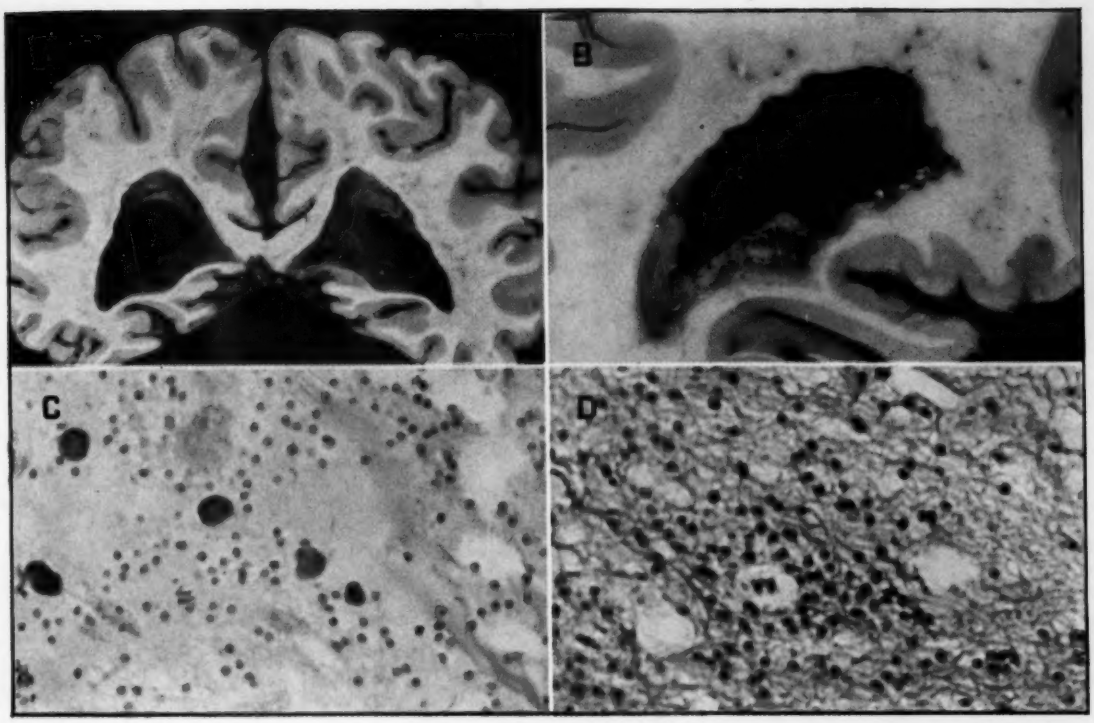

Fig. 1.—*A*, frontal section of brain through the splenium of the corpus callosum. Note the nodular masses of tumor in the posterior horns of the lateral ventricles.

B, frontal section of brain through the posterior horn of the left lateral ventricle. Note focal loss of line of demarcation between the tumor in the ventricle and the white matter. There is a small nodule of tumor in the leptomeninges over the lingual gyrus.

C, portion of partially degenerated tumor from the left lateral ventricle, stained with mucicarmine. Note the weakly positive reaction for mucin and the basophilic concrements. × 130.

D, tissue removed from between the optic chiasm and the tuber cinereum at the second operation, stained with mucicarmine. Some of the fibrils and cell processes are deep red. × 130.

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because of a period of more severe and numerous "spells," showed focal calcifications in the anterior ends of the inferior horns of both lateral ventricles and the posterior horn of the left lateral ventricle. On March 3, 1944 he returned because of inability to focus his eyes. During the next week there developed dizziness, tinnitus, nausea and convulsive seizures, which started in either foot and spread to the rest of the body. There were slight wasting of muscles, widespread hypotonia, absence of abdominal reflexes, sluggish knee jerks, ataxia and bilateral optic nerve atrophy. An encephalogram showed the same changes as before. A left frontal craniotomy was done on March 23. A thin-walled cyst ruptured and collapsed as the left frontal lobe was elevated, exposing a small mass of reddish gray tissue posterosuperior to the optic chiasm. A portion of this

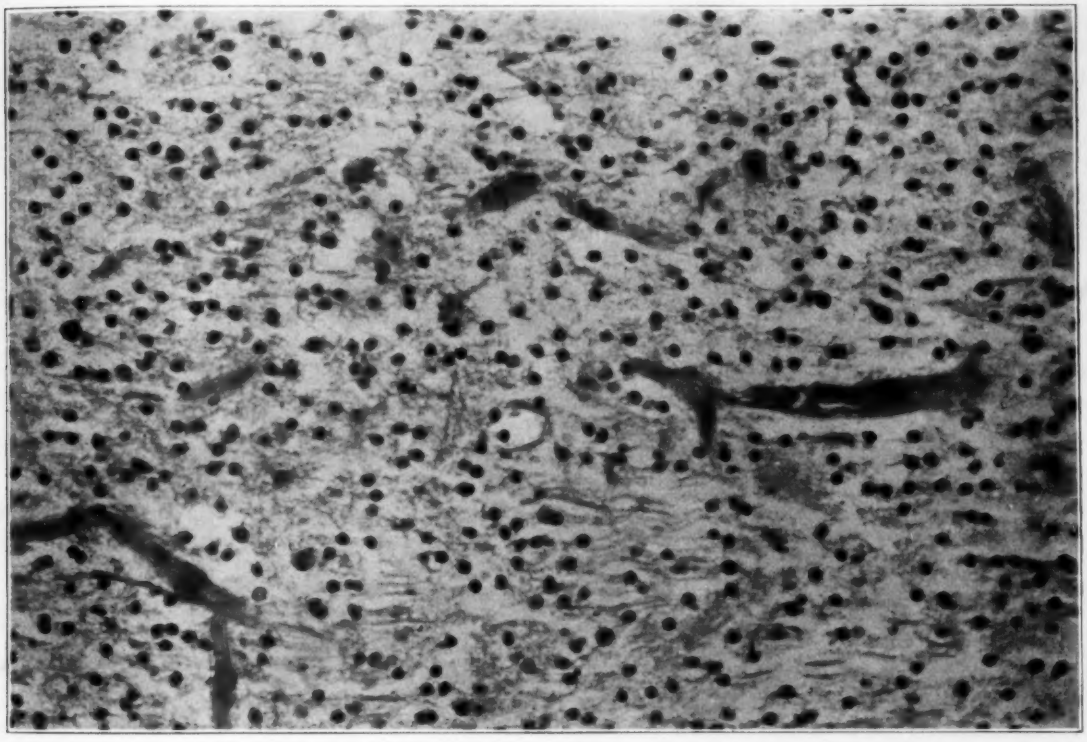

Fig. 2.—A portion of tumor from the right superior recess of the fourth ventricle. The nuclei are almost uniform in size, shape, staining reaction and distribution. The cytoplasm is not sharply delimited. Some of the cells are united by indistinct processes. Hematoxylin and eosin. × 415.

was removed. The patient died twenty-four hours after operation, thirteen years and seven months after his first admission to the hospital.

Autopsy, complete except for examination of the spinal cord, was performed sixteen hours after death by Dr. J. C. Sherrick. Observations on the brain and related structures will be given in detail. The lesions noted in the remainder of the body were as follows: slight atrophy of the thyroid gland; healed, nondeforming endocarditis of the aortic, mitral, pulmonic and tricuspid valves; slight arteriosclerosis of the aorta; slight hyperemia and edema of the lungs; primary tuberculous complex of the lower lobe of the left lung and the left inferior bronchopulmonary lymph nodes; active miliary tubercles in the liver, spleen and an accessory spleen, and slight atrophy of the testes. The thyroid gland weighed 17 Gm. and consisted of follicles of average size, filled with colloid and lined with simple low cuboidal to flat epithelium. Each testis, with the epididymis, weighed 14 Gm. A majority of the contorted seminiferous tubules showed few or no sperm heads, a reduced number of spermatids, spermatocytes and spermatogonia and an increased number of sustentacular cells. Some tubules were lined only with sustentacular cells. The interstitial cells were of average type.

The scalp, calvaria and dura showed recent and remote surgical wounds, but no trace of the remote left parieto-occipital fracture. The brain weighed 1,560 Gm. The leptomeninges were slightly thickened and reddened along the choroidal and the first part of the sylvian fissures, around the pineal and the adjacent midbrain, in the interpeduncular fossa and around the foramens of Luschka. A blood clot and friable reddish gray tissue obscured the floor of the third ventricle back to the mamillary bodies. The gyri were flattened and the sulci narrowed. The sella was enlarged; the posterior clinoid processes were eroded, and the pituitary was flattened. Section of the brain, after fixation in solution of formaldehyde U. S. P. and saline solution, revealed marked dilatation of the lateral ventricles; the third ventricle was moderately and the fourth slightly enlarged. Patches of a thin to thick layer of reddish gray, semitranslucent, soft, gelatinous material occurred on the walls of all the ventricles (fig. 1 *A* and *B*). It could be scraped from the ependymal surface with ease. The foramens of Monro were slightly narrowed, and the aqueduct of Sylvius to a greater degree by similar material, which also partially obscured but was readily separated from the choroid plexuses. In the surfaces made by section the boundary

between this material and the underlying brain was irregular in several places, notably in the region of the head of the right caudate nucleus and the right superior recess of the fourth ventricle. There was no demonstrable hypothalamus, the floor of the third ventricle being replaced by gelatinous material and blood clot.

Sections from many portions of the brain containing gelatinous material were stained with hematoxylin and eosin, Holzer's method for glia fibrils and Bodian's method for neurofibrils. Later, preparations were made with Mayer's mucicarmine stain and Penfield's combined method for oligodendroglia and microglia.

All involved portions showed abnormal tissue, interpreted as tumor, which varied in structure within a narrow range. The cells, moderately numerous to sparse, formed a reticulum in some parts, with granular, fibrillar and homogeneous eosinophilic intercellular material (fig. 2). There was slight, incomplete lobulation by slender septums, which contained small vessels formed principally of a layer of endothelium. Foci of hemorrhage were common. The tumor cells had scant, ill defined, granular, eosinophilic cytoplasm. Some had processes. The nuclei were of almost uniform size, small, round or oval, and slightly hyperchromatic, with thin membrane and regularly dispersed small chromatin granules. Some nuclei showed one or two coarser granules, but in none was an eosinophilic nucleolus noted. No mitotic figures were seen. Readily identifiable astrocytes occurred in small numbers, chiefly where the tumor involved brain tissue. Such foci were more numerous than was apparent grossly, their widespread, superficial character suggesting invasion from ventricular growth. Degeneration and necrosis were marked in portions from within the ventricles. Concrements, 25 to 500 microns in diameter, spherical or irregular, and some laminated, were numerous in ventricular portions and much less common elsewhere (fig. 3). They were more commonly basophilic and when treated by von Kossa's method gave a positive reaction for calcium. Mucicarmine preparations showed faint to deep red staining of fibrillar material but only a few patches of light pink homogeneous substance (fig. 1 *C*). Frozen sections prepared by Penfield's modification of Hortega's method for oligodendroglia (Mallory [14]) gave corroborative evidence that the tumor cells were mainly oligodendrocytes. They were impregnated about as deeply as the normal oligodendrocytes in the brain; the nuclei were similar in appearance, and an occasional cell had a few short processes (fig. 4). Astrocytes were faintly impregnated, larger, more richly branched and fibrillated. Holzer preparations showed glia fibers in the regions containing astrocytes.

In the first surgical specimen, removed in 1930, there were small groups of cells with uniform, round, finely granular nuclei in collagenous fibrous tissue. The rest of the material was stained with mucicarmine but lacked the cells with round nuclei. The second surgical specimen was identical in appearance with the tumor seen at autopsy (fig. 1 *D*).

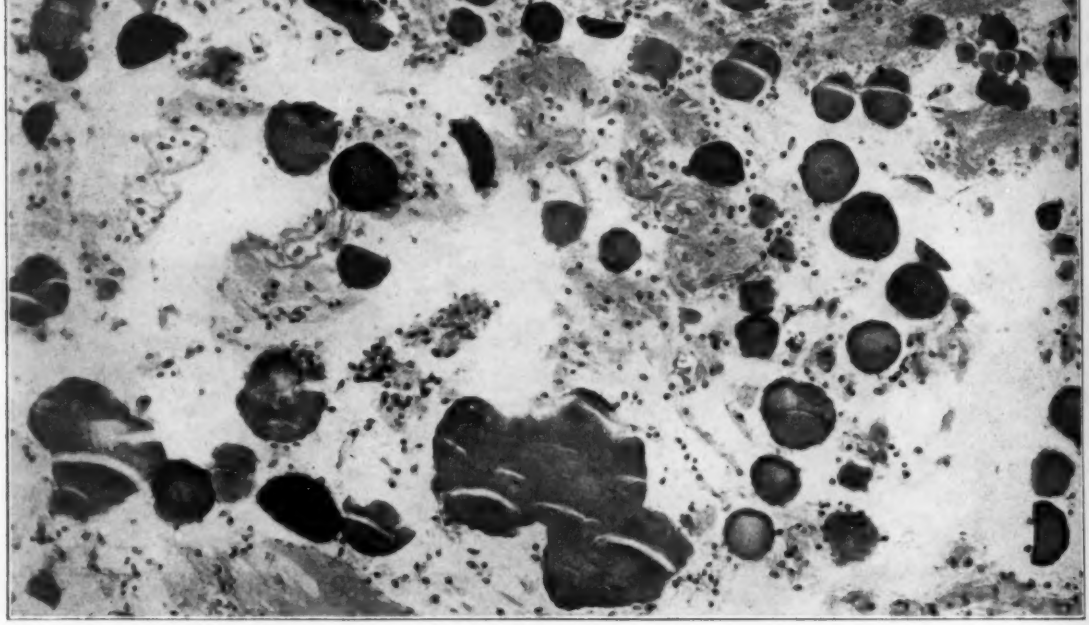

Fig. 3.—A portion of tumor from within the posterior horn of the right lateral ventricle. In addition to the numerous concrements, note the greater dispersion of the tumor cells. Material in some of these spaces stained feebly with mucicarmine. Some of the cell processes were deeply stained. Hematoxylin and eosin. × 210.

14. Mallory, F. B.: Pathological Technique, Philadelphia, W. B. Saunders Company, 1938, p. 254.

COMMENT

The tumor in this case is considered to be an oligodendroglioma. The nuclei were like those of oligodendrocytes.[15] The cytoplasm contained no fibrils. In Hortega preparations the tumor cells were impregnated about as deeply as the normal oligodendrocytes, and some showed a few short processes. There was a questionably positive reaction for mucin. The tumor occurred on the walls of all the ventricles, involved the brain substance superficially in many places and was identified in the leptomeninges around the hypothalamus, the beginning of the sylvian fissures and just outside the foramens of Luschka.

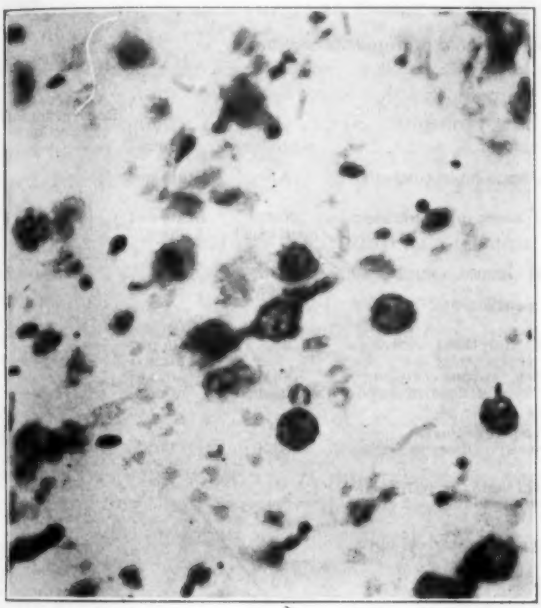

Fig. 4.—Intraventricular portion of tumor, prepared according to Penfield's modification of del Río Hortega's method for oligodendroglia. At about the center is a cell with two thick processes which leave the plane of focus. The nuclei of these cells are identical in appearance with those of well impregnated oligodendrocytes in the brain. × 1,245.

In textbooks and monographs dealing with the clinical or pathologic aspects of gliomas, such as those by Biggart[16]; Bailey[17]; Bailey and Cushing[3]; Bucy[18]; Cushing[19]; Elvidge, Penfield and Cone,[10] and Weil,[20] no mention is made of dissemination of oligodendroglioma. Hassin[21] referred briefly to a case of Kwan and Alpers[22] in which tumor occurred in the leptomeninges of the sylvian fissure after removal of a tumor in the frontal region.

Observations on the spread of gliomas are not numerous, probably in part the result of syllogistic reasoning. The presence of spinal metastases in a case of cerebral glioma led Cairns and Russell[23] to include removal of the spinal cord in the next 22 autopsies in cases of cerebral glioma. They found spinal subarachnoid metastases in 8 cases, in 3 of which the tumor was a medulloblastoma, in 1 an astrocytoma, in 1 an ependymal glioma, in 1 a glioblastoma multiforme, in 1 a neuroepithelioma of the retina and in 1 an unclassified glioma. Nelson[24] described an instance of histologically verified metastases of medulloblastoma to the centrums of thoracic vertebrae, emphasizing the accidental nature of the observation. Van Wagenen[25] noted widespread ependymal implantation of papilloma of the choroid plexus, a condition present in 5 of 45 cases he collected from reports by others. That medulloblastoma frequently is disseminated through the subarachnoid space is well known. That such spread is not rare with other gliomas is less well known.

Brief comments indicating that oligodendroglioma may be less benign than is usually thought were made by Cushing,[19] Eisenhardt[26] and Elvidge, Penfield and Cone.[10] This is surprising, in view of a series of reports which began shortly after Bailey and Cushing[3] first presented the entity of oligodendroglioma. Dickson,[4] in 1926,

15. Dr. Percival Bailey examined the hematoxylin and eosin preparations and stated that the tumor cells, because of the structure of the nuclei, were probably oligodendrocytes.

16. Biggart, J. H.: Pathology of the Nervous System, Baltimore, William Wood & Company, 1936, pp. 263-265.

17. Bailey, P.: Cellular Types in Primary Tumors of the Brain, in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 3, sect. 18, pp. 941-942.

18. Bucy, P. C.: Tumors of the Brain, in Tice, F.: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc., 1921, vol. 9, p. 663.

19. Cushing, H.: Intracranial Tumours, Springfield, Ill., Charles C Thomas, Publisher, 1932.

20. Weil, A.: A Text-Book of Neuropathology, Philadelphia, Lea & Febiger, 1933.

21. Hassin, G. B.: Histopathology of the Peripheral and Central Nervous System, ed. 2, New York, Paul B. Hoeber, Inc., 1940, pp. 484-487.

22. Kwan, S. T., and Alpers, B. J.: The Oligodendrogliomas, Arch. Neurol. & Psychiat. **26**:279-321 (Aug.) 1931.

23. Cairns, H., and Russell, D. S.: Intracranial and Spinal Metastases in Gliomas of the Brain, Brain **54**: 377-420, 1931.

24. Nelson, A. A.: Metastases of Intracranial Tumors, Am. J. Cancer **28**:1-12, 1936.

25. Van Wagenen, W. P.: Papillomas of the Choroid Plexus, Arch. Surg. **20**:199-231 (Feb.) 1930.

26. Eisenhardt, L.: Long Postoperative Survivals in Cases of Intracranial Tumor, A. Research Nerv. & Ment. Dis., Proc. (1935) **16**:390-416, 1937.

described an oligodendroglioma of the floor of the third ventricle which involved the leptomeninges of the interpeduncular fossa. Cairns,[27] in 1929, reported the presence of tumor deposits in the posterior horns of the lateral ventricles, the left foramen of Monro and the fourth ventricle approximately three and a half years after operative removal of an oligodendroglioma from the right frontal lobe. In 1931, Martin [28] reported diffuse ventricular spread about one year after removal of a left parietal oligodendroglioma. There was a nodule of tumor in the scalp just anterior to a cerebral hernia at the site of operation. Also in 1931, Kwan and Alpers [22] presented 4 cases of oligodendroglioma, in 1 of which a nodule of tumor was noted in the leptomeninges of the left sylvian fissure at autopsy fourteen months after removal of a left frontal tumor. Kernohan,[29] in 1932, noted recurrence and subarachnoid spread in only 1 of 52 cases of tumor of the spinal cord, that of an oligodendroglioma. A similar tumor of the filum terminale, only partially removed, recurred not only with subarachnoid spread but with invasion of skeletal muscle bordering on the wound. Greenfield and Robertson,[30] in 1933, described 5 cases of oligodendroglioma. In 2 there were ventricular deposits and in 1 subarachnoid, as well as ventricular, spread. Löwenberg and Waggoner,[13] in 1939, from a study of 21 cases, stated, "the oligodendrogliomas have a definite tendency to invade the leptomeninges, and in some cases also the pachymeninges"; and, from a study of the literature, "oligodendrogliomas in general tend to invade the ventricular system." Finally, Beck and Russell,[31] in 1942, presented 4 cases in which occurred diffuse spread of oligodendroglioma through the subarachnoid space, with ependymal deposits in 3 of them, for which they coined the term "oligodendrogliomatosis of the cerebrospinal pathway." They stressed the presence of mucinous degeneration of the tumor as a feature of diagnostic importance. The basis for the presence of mucin lies in the tendency of oligodendroglia undergoing degeneration to form mucin, as shown by Grynfeltt,[32] by Bailey

Data in Twelve Cases of Disseminated Oligodendroglioma

Author	Age at Death, Years	Sex	Duration, Years	Site of Tumor	Hydrocephalus	Mucin	Calcification Roentgenogram	Calcification Section
Dickson [4]	6	M	½	Hypothalamus; basal cistern; interpeduncular fossa	All	Stain not done	−	−
Martin [28]	44	M	4	Left parietal and occipital lobes; all ventricles; scalp (operative site)	Not mentioned	Stain not done	+	+
Greenfield and Robertson [30]	16	F	1	Third ventricle and iter	1, 2 and 3	+	−	−
	44	M	¾	Right frontal lobe; right lateral, third and fourth ventricles	Not mentioned	+	−	−
	50	F	7	Iter; fourth ventricle; pontile and basilar cisterns	All	+	−	−
Löwenberg and Waggoner [13]	17	M	?	Septum pellucidum; lateral and third ventricles	1 and 2	Stain not done	−	−
	51	F	14	Septum pellucidum, fornices, corpus callosum, tuber cinereum, all ventricles, diffuse in leptomeninges, parts of cortex	Not mentioned	Stain not done	−	−
Beck and Russell [31]	36	M	7	All ventricles; diffuse in leptomeninges	All	+	−	−
	42	M	1½	Tuber cinereum; all ventricles; diffuse in leptomeninges	All	+	−	−
	6	F	½	Right frontal lobe; lateral and fourth ventricles; diffuse in leptomeninges; dura of right frontal region	All	+	+	Not mentioned
	4	F	½	Diffuse in leptomeninges; cerebellar cortex, optic chiasm	All	+	−	−
Blumenfeld and Gardner	31	M	14	Hypothalamus; all ventricles; focal in leptomeninges	All	±	+	+

27. Cairns, H.: A Study of Intracranial Surgery, Medical Research Council, Special Report Series no. 125, London, His Majesty's Stationery Office, 1929.

28. Martin, J. P.: Two Cases of Oligodendroglioma with Remarks on the General Clinical Features of Such Cases, Brain **54**:330-349, 1931.

29. Kernohan, J. A.: Primary Tumors of the Spinal Cord and Intradural Filum Terminale, in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 3, sect. 20, pp. 1014-1015.

30. Greenfield, J. G., and Robertson, E. G.: Cystic Oligodendrogliomas of the Cerebral Hemispheres and Ventricular Oligodendrogliomas, Brain **56**:247-264, 1933.

31. Beck, D. J. K., and Russell, D. S.: Oligodendrogliomatosis of the Cerebrospinal Pathway, Brain **65**:352-372, 1942.

32. Grynfeltt, E.: Mucocytes et leur signification dans les processes d'inflammation chronique des centres cérébrospinaux, Compt. rend. Soc. de biol. **89**: 1264-1266, 1923.

33. Bailey, P., and Schaltenbrand, G.: Die muköse Degeneration der Oligodendroglia, Deutsche Ztschr. f. Nervenh. **97**:231-237, 1927.

and Schaltenbrand,[33] by Grinker and Stevens [34] and by others.

Eleven cases have been collected from reports by other authors in which the tumor showed ventricular or meningeal dissemination or both, exclusive of cases in which dissemination was limited to the region traversed by operation. Pertinent data are given in the accompanying table. The duration of clinically recognized disease varied from one-half to fourteen years. Of the 12 cases, headache occurred in 11; various visual disturbances were present in 9; nausea, vomiting or both was experienced in 9, and disturbances of mentality or personality were exhibited in 8. Hydrocephalus was present in 9 cases. Tumor involved the ependyma in 11 cases and the leptomeninges in 8 cases. Stains for mucin were made in 8 cases, with a questionable or weakly to strongly positive reaction in all. In none did the stain for mucin give definitely negative results. Calcification appeared in 4 cases—in both roentgenograms and sections in 2, in roentgenograms only in 1 and in sections only in 1.

There are no distinctive symptoms or signs. Two observations may prove helpful in making a diagnosis. If, at operation, there is focal or diffuse thickening of the leptomeninges, a stain for mucin should be made on a biopsy specimen, and a portion should be properly fixed for the del Río Hortega method. Foci of calcification within the ventricles should suggest this tumor.

The frequent presence of this tumor on and in ependyma lends support to the cell lineage schemes of Kernohan and Fletcher-Kernohan [35] and of Globus and Kuhlenbeck.[36] The former derived oligodendroglia from primitive ependymoepithelium, because of the presence in cellular ependymomas of cells morphologically indistinguishable from oligodendrocytes. The latter suggested that oligodendroglia may be derived from spongioblasts or bipotential mother cells of the subependymal cell plate.

34. Grinker, R. R., and Stevens, E.: Mucoid Degeneration of the Oligodendroglia and the Formation of Free Mucin in the Brain, Arch. Path. **8**:171-179 (Aug.) 1929.

35. Kernohan, J. A., and Fletcher-Kernohan, E. M.: Ependymomas: A Study of 109 Cases, A. Research Nerv. & Ment. Dis., Proc. (1935) **16**:182-209, 1937.

36. Globus, J. H., and Kuhlenbeck, H.: The Subependymal Cell Plate (Matrix) and Its Relationship to Brain Tumors of the Ependymal Type, J. Neuropath. & Exper. Neurol. **3**:1-35, 1944.

SUMMARY

The man whose case is reported herein, 31 years old at the time of his death, had an oligodendroglioma in the cerebral ventricles for at least fourteen years. The tumor apparently originated in and subsequently destroyed the hypothalamic region. Early in its course it involved the basilar leptomeninges.

Data from the case and from 11 other cases reported in the literature showed that the time elapsing between onset of symptoms and death varied from one-half to fourteen years. Localizing symptoms and signs were absent in most cases. In three fourths or more of the cases headaches, visual disturbances, mental abnormalities, personality changes, nausea, vomiting or hydrocephalus occurred. The ependyma was involved in 11 cases and the leptomeninges in 8. Mucin was questionably or definitely present in the tumor in all cases in which a special stain was made. The morphologic features of the tumor in the leptomeninges may be obscured by fibrosis, in which instance a stain for mucin may be of value. Focal calcification of the tumor occurred in 4 cases and was demonstrated roentgenographically in 3 of these. Focal calcification seen in the ventricles roentgenographically should suggest ventricular oligodendroglioma.

Data from this case, and from other reported cases, furnish a basis for the opinion that oligodendroglioma may be neither as localized nor as slow growing as is usually thought. In its tendency to become disseminated through the cerebrospinal pathway oligodendroglioma is exceeded only by medulloblastoma.

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Ninety-Third Street and Euclid Avenue.

BLOOD SUPPLY OF PERIPHERAL NERVES

PRACTICAL CONSIDERATIONS

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The blood supply of the larger peripheral nerves in man has been described in considerable detail in two prevous publications (Sunderland [1]). The purpose of the present communication is to outline briefly certain refinements of operative technic which are suggested by the anatomic study of the arrangement and distribution of the arteriae nervorum and which may prove of value in effecting improvements in surgical procedures carried out on peripheral nerves. The reader is referred to the previous two papers for details concerning the general and topographic features of the blood supply of the individual peripheral nerves.

It has been demonstrated that in certain regions along its course a nerve is often securely and intimately attached to an adjacent arterial channel by short nutrient arteries. Examples are provided by the ulnar nerve in the condylar groove and in the distal two thirds of the forearm; by the sciatic nerve, which is frequently securely attached to the perforating anastomotic arterial chain in the thigh, and by the anterior and posterior tibial nerves in the leg. The free and extensive mobilization of nerves is frequently required in peripheral nerve surgery, either to permit the transposition of the nerve to a new bed or, when it is being separated from surrounding attachments, to facilitate approximation of the ends after the loss of a segment. Such procedures obviously necessitate the division of any arteriae nervorum which bind the nerve to an accompanying major arterial channel, and on occasion this does involve the sacrifice of many large nutrient vessels. The question which naturally arises is whether or not such a loss will jeopardize, seriously or otherwise, the nutrition of the nerve.

Fortunately, each peripheral nerve is abundantly vascularized throughout its entire length by a succession of vessels which, by their repeated division and anastomosis on and within the nerve, outline an unbroken intraneural vascular net. A distinctive feature of this pattern is the considerable overlap of supply which obtains between the nutrient arteries entering at different levels. It is also common to see one or several longitudinally arranged macroscopic vessels, arteriolar in type, on the surface of large peripheral nerves. These superficial longitudinal channels, which are of variable, but often extensive, length, are reenforced at intervals by new arteriae nervorum. The profuse anastomosis insured by this arrangement renders it unlikely that any nutrient artery will dominate the intraneural circulation in any particular segment of a nerve.

During this investigation nerves have frequently been stripped at operation of all surrounding connections for distances of up to 15 cm., and yet when the nerve was divided distally the cut end of the freed section continued to bleed. Preparatory to its transposition anterior to the humeral epicondyle, the ulnar nerve has been mobilized over corresponding distances without in any way retarding or impairing the improvement in conduction which usually follows such a procedure. The experimental work of Adams,[2] who has recently investigated the effects of exclusion of the regional sources of supply on the sciatic nerve of the rabbit, and the investigations of Bentley and Schlapp [3] on the blood supply of nerves in the cat support this belief in the efficiency of the collateral circulation in the nerve. The problem, however, assumes importance when all the vessels to a nerve are affected simultaneously in a generalized sclerosing condition. The establishment of an effective collateral circulation is then no longer possible, and the conducting elements consequently suffer.

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1. Sunderland, S.: The Blood Supply of the Nerves of the Upper Limb in Man, Arch. Neurol. & Psychiat. **53**:91 (Feb.) 1945; The Blood Supply of the Sciatic Nerve and Its Popliteal Divisions in Man, ibid., this issue, p. 283.

2. Adams, W. E.: The Blood Supply of Nerves: II. The Effects of Exclusion of Its Regional Sources of Supply on the Sciatic Nerve of the Rabbit, J. Anat. **77**:243, 1943.

3. Bentley, F. H., and Schlapp, W.: Experiments on the Blood Supply of Nerves, J. Physiol. **102**:62, 1943.

Admittedly, there are occasions, though they are infrequent, when one nutrient artery would appear to supply long stretches of a nerve without reenforcement, but it has been found, from an examination of sectioned and injected material, that even under these apparently adverse conditions of supply the anastomosis is of such dimensions at the peripheral limits of the solitary channel that there is only a remote possibility that segmental ischemia would result from the blocking of such a single nutrient vessel.

The manner in which the arteriae nervorum are divided when one is freeing the nerve is of some significance. In the event of the obstruction of one or more entering nutrient vessels, the circulation is maintained by vessels coursing in the crevices between the fasciculi and the large longitudinal anastomosing channels on the surface of the nerve. Should the superficial system be interrupted, vascularization of the nerve then depends solely on the collateral circulation established by the intraneural pattern within the nerve, and the vessels composing the latter are not always as large as those on the surface. Consequently, when one is stripping the nerve from its surroundings, it is advisable to preserve, wherever possible, the superficial longitudinal pathway. Reference to the accompanying diagram (figure) will make this point clear. The superficial pathway will be preserved if the nutrient vessels are divided as far from the nerve as is possible and convenient (at point *A*) and before they have branched into their ascending and descending limbs. If the nerve is roughly and carelessly dissected or stripped from its bed, these delicate channels are likely to be torn at the site where they enter the nerve (at points *B*), interrupting thereby the superficial system on the surface of the nerve, a disturbance which, in turn, is liable to embarrass the intraneural circulation. Where there is more than one superficial longitudinal channel, which is often the case, the destruction of one can be adequately compensated for, but the presence of such multiple superficial channels cannot be relied on.

The appropriate disposal of the arteriae nervorum when one is freeing a nerve from adjacent tissues is often greatly aided by a knowledge of the regional sources of supply to the nerve and the point at which the latter is usually securely anchored to adjacent arteries by short, stout arteriae nervorum. Furthermore, should a large nutrient vessel be torn or inadvertently divided at the surface of the nerve, it may retract into the epineurium and cause troublesome hemorrhage, while attempts to secure the vessel may cause damage to superficial fasciculi. Such a complication can be avoided by planned ligation of the vessels at some distance from the nerve.

It is customary to execute operations on peripheral nerves under tourniquet control. Under such conditions nutrient arteries may be severed and retracted unnoticed within the nerve. These may bleed postoperatively into the intraneural tissues and subsequently result in scarring, which, in turn, may imperil nerve fibers. Since large vessels on and within the nerve are occasionally severed when freshening nerve ends preparatory to suture, it is advisable to release

Superficial blood supply of the peripheral nerve.

the tourniquet during this procedure in order to determine whether any substantial "bleeders" are presenting at the nerve ends. If hemorrhage reaches proportions which demand mechanical control, it is important to remember that any but the most delicate attempts to secure the severed vessels will inevitably result in damage to the fasciculi. It is conceivable that failure to control extensive bleeding at and about the suture line may ultimately lead to scarring and thereby introduce an additional factor in retarding and limiting regeneration. Capillary bleeding is usually controlled by the suture, but even

here postoperative oozing may lead to similar complications.

Intraneural hemorrhage can reach considerable proportions in the sciatic nerve (where the main intraneural channels are often of large caliber), and this may be one of the factors leading to irreparable changes in the nerve following trauma which does not result in any break in continuity of the nerve. There is also some evidence (personal observations) to suggest that occasionally fusiform swellings on the nerve at the site of injury are partly the result of the organization of hematomas which have split and separated the fasciculi.

The manner in which the large arteries and nerves of a limb may be closely and tightly knit into a common neurovascular bundle should also be borne in mind when ligating arteries—it is not unknown for the inexperienced to ligate the nerve with the artery.

The anastomoses, on and within the nerve, between nutrient arteries derived from different and widely separated major arteries form the basis for the development of collateral circulations when the major arterial channel to a limb has been interrupted. Collateral circulations of this type and their importance in maintaining the circulation of the limb have been reported on by various investigators (Porta,[4] Holl,[5] Hyrtl,[6] Zuckerkandl,[7] Quénu and Lejars,[8] Tonkoff,[9] Makins [10]).

4. Porta, L.: Delle alterazioni patologiche delle arterie per la legatura e la torsione, esperienze ed osservazioni, Milan, G. Bernardoni di Gio, 1845; cited by Tonkoff.[9]

5. Holl, M.: Zerreissung der Kniekehlen—Gefasse und Nerven bei Streckung einer Kontraktur, Arch. f. klin. Chir. **22**:374, 1878; Verrenkung des linken Ellbogengelenkes mit Zerreissung der A. ulnaris und der N. medianus und ulnaris; Heilung; Collateral-Kreislauf, Med. Jahrb., 1880, p. 151.

6. Hyrtl, J.: Lehrbuch der Anatomie des Menschen, Vienna, W. Braumüller, 1881.

7. Zuckerkandl, O.: Zwei Fälle von Collateralkreislauf, Med. Jahrb. **15**:273, 1885; cited by Poirier, P., and Charpy, A.: Traité d'anatomie humaine, ed. 2, Paris, L. Battaille & Cie, 1901, vol. 3, p. 633.

8. Quénu, J., and Lejars, F.: Etude anatomique sur les vaisseaux sanguins des nerfs, Arch. de neurol. **23**:1, 1892.

9. Tonkoff, W.: Die Arterien der Intervertebralganglien und der Cerebrospinalnerven des Menschen, Internat. Monatschr. f. Anat. u. Physiol. **15**:353, 1898.

10. Makins, G. H.: Gunshot Injuries to Blood Vessels, Bristol, J. Wright & Sons, 1919.

BLOOD SUPPLY OF THE SCIATIC NERVE AND ITS POPLITEAL DIVISIONS IN MAN

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The results of an anatomic study of the blood supply of the peripheral nerves of the upper limb in man have been described in a previous paper (Sunderland [1]). The investigation which forms the subject of the present report represents an extension of those studies and covers the blood supply of the sciatic nerve and its popliteal divisions.

REVIEW OF LITERATURE

Information concerning the blood supply of the sciatic nerve and its divisions is contained in the works of Haller,[2] Walter,[3] Hyrtl,[4] Henle,[5] Holl,[6] Quénu and Lejars,[7] Bartholdy,[8] Tonkoff,[9] Chaumet, Heymann and Mouchet,[10] Portal,[11] Rauber [12] and Sappey.[12] Their descriptions are, however, with the exception of those by Tonkoff and Bartholdy, brief and incomplete and cover only sections of the nerve. The present investigation was undertaken to extend the observations of Tonkoff and Bartholdy and was based on a much larger series of adult specimens than has hitherto been examined. Their results can be most appropriately reviewed in the sections of the text devoted to a description of the regional sources of supply to the nerve.

MATERIAL

Observations were made on the nutrient arteries to the sciatic nerve and its popliteal divisions in 40 adult dissected specimens. In each specimen the nerves were examined from the point where the sciatic nerve emerged from the pelvis to the level of the malleoli. The arrangement of the intraneural vascular pattern was studied microscopically in histologic sections prepared from segments of the nerves taken at the following levels: gluteal region; upper, middle and distal thirds of the thigh; popliteal fossa; neck of the fibula, and upper, middle and distal thirds of the lower portion of the leg.

EXTRANEURAL AND INTRANEURAL VASCULAR PATTERN

Reference should be made to the original paper (Sunderland [1]) for a detailed account of the general features relating to the extraneural and intraneural disposition of the vasa nervorum, since these have a general application which covers the sciatic nerve. The following additional features are worthy of note in connection with the angioarchitecture of this nerve and its divisions:

1. The largest arteriae nervorum observed in the upper and lower limbs were those supplying the sciatic nerve in the buttock and thigh. They were arteriolar in type and were provided by the inferior gluteal artery and the perforating anastomotic chain.

2. As in the upper limb, nutrient arteries of the direct type predominated; the number of the indirect type in the leg exceeded that in the thigh and buttock.

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1. Sunderland, S.: The Blood Supply of the Nerves of the Upper Limb in Man, Arch. Neurol. & Psychiat. **53**:91 (Feb.) 1945.

2. Haller, A.: Icones anatomicae quibus præcipue aliquæ partes corporis humani delineatæ proponuntur et arteriarum potissimum historia continetur, Göttingen, A. Vanderhoeck, 1756.

3. Walter, F. A.: Angiologisches Handbuch, zum Gebrauch seiner Zuhörer, Berlin, G. A. Lange, 1789; cited by Bartholdy.[8]

4. Hyrtl, J.: Ueber normale und abnorme Verhältnisse der Schlagadern des Unterschenkels, Vienna, K. Gerold's Sohn, 1864.

5. Henle, J.: Handbuch der systematischen Anatomie des Menschen, Braunschweig, F. Vieweg u. Sohn, 1868, vol. 3, pt. 1.

6. Holl, M.: Zerreissung der Kniekehlen-Gefässe und Nerven bei Streckung einer Kontraktur, Arch. f. klin. Chir. **22**:374, 1878.

7. Quénu, J., and Lejars, F.: Étude anatomique sur les vaisseaux sanguins des nerfs, Arch. de neurol. **23**:1, 1892.

8. Bartholdy, K.: Die Arterien der Nerven, Morphol. Arb. **7**:393, 1897.

9. Tonkoff, W.: Die Arterien der Intervertebralganglien und der Cerebrospinalnerven des Menschen, Internat. Monatschr. f. Anat. u. Physiol. **15**:353, 1898.

10. Chaumet, G.; Heymann, and Mouchet: Note sur la topographie des artères des nerfs sciatiques, Bull. et mém. Soc. anat. de Paris **18**:404, 1921.

11. Portal, A.: Cours d'anatomie médicale, Paris, Baudouin, 1804, vol. 3; cited by Bartholdy.[8]

12. Cited by Tonkoff.[9]

3. The T-shaped division was the most common pattern assumed by a nutrient artery when it reached the nerve. In the case of the arteries provided by the crucial anastomosis and the branches from the perforating arteries, the ascending limb of the T was often larger than the descending limb. This was uncommon in the arm.

4. Though large nutrient vessels were occasionally observed descending for long distances on the surface of the sciatic trunk, such vessels usually entered the nerve either immediately on reaching it or after a short course on its surface. They then passed to the interval between the two divisions and as they descended branched into the interfascicular spaces (fig. 1 *A*).

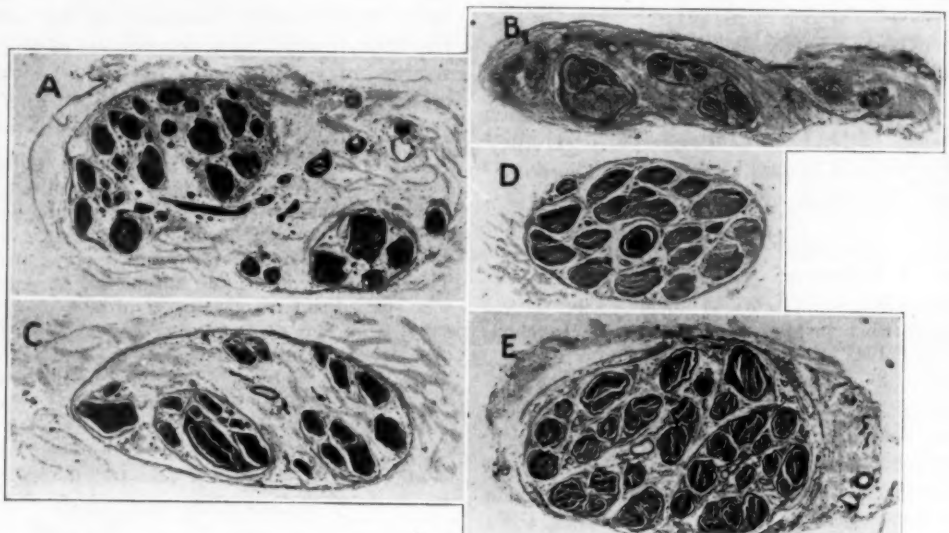

Fig. 1.—*A*, photomicrograph (× 6) of a transverse sciatic nerve in the thigh, illustrating the presence of multiple major arterial channels between its two divisions and the mode of branching into the fasciculi; *B*, photomicrograph (× 4.5) of a transverse section of the lateral popliteal nerve at the neck of the fibula, demonstrating (a) the thinning and flattening of the trunk, (b) the presence of many fasciculi and (c) the exposed position of the nutrient vessels (88 per cent of specimens); *C*, photomicrograph (× 8) of a transverse section of the lateral popliteal nerve at the neck of the fibula, demonstrating the central position occupied by the major nutrient channels (12 per cent of specimens); *D*, photomicrograph (× 8) of a transverse section of the posterior tibial nerve, showing a centrally situated major arterial channel (this is the common arrangement), and *E*, photomicrograph (× 8) of a transverse section of the posterior tibial nerve, showing a peripherally situated major arterial channel (this is an unusual arrangement).

5. In the popliteal fossa the largest arterial channels coursed on or within the nerve. As the lateral popliteal (common peroneal) nerve approached the neck of the fibula, the major intraneural vessels were observed to occupy a superficial and exposed position in 88 per cent of the specimens and a deep and protected position between the fasciculi in only 12 per cent (fig. 1 *B* and *C*). The disposition of the nutrient vessels and fasciculi in this region is of special significance.

In an investigation of the paralysis induced by direct pressure and by tourniquet in the sciatic nerve of the cat, Denny-Brown and Brenner [13] observed that the lesions produced in their experiments were maximal in the peroneal division just below the bifurcation of the sciatic nerve. They compared this observation with the reported differences in vulnerability of the medial and the lateral popliteal nerve in man to apparently similar injurious agents and explained the relative susceptibility of the two branches as follows:

> Besides the obvious difference in size of the two nerves, the peroneal division is usually in the form of one major bundle, so that its vessels have less protection than those of the popliteal division, which lie in the crevices between the bundles. This anatomic difference may certainly account for the difference in lesions caused by pressure.

They did not, however, make it clear whether their explanation applied to man, to the cat or to both.

In no specimen in the present investigation was the lateral popliteal nerve composed of a single bundle. Furthermore, there was no fea-

13. Denny-Brown, D., and Brenner, C.: Paralysis of Nerve Induced by Direct Pressure and by Tourniquet, Arch. Neurol. & Psychiat. **51**:1 (Jan.) 1944.

ture of the intraneural vascular pattern which was specific to this nerve or which would adequately account for the susceptibility of this nerve to pressure. In a recent investigation devoted to a study of the adipose tissue content of peripheral nerves (to be reported elsewhere), it has been demonstrated that the lateral division of the sciatic nerve and the lateral popliteal nerve usually contain less supporting adipose tissue than the medial division and the medial popliteal nerve, and I am convinced that this morphologic difference provides a more satisfactory explanation for the susceptibility of this nerve to pressure.

At the neck of the fibula the lateral popliteal nerve was usually flattened and thined against a firm, resistant surface, was composed of many small fasciculi, was commencing to separate into its divisions and, as a rule, contained very little supporting adipose tissue. In addition, the associated nutrient vessels usually occupied an exposed or relatively exposed position (fig. 1 *B*). I believe that it is a combination of these morphologic features which predisposes the nerve to compression injuries at this site.

6. As a rule the intraneural plexus in the buttock and thigh contained several arterial channels of fairly large caliber whereas below the knee one major vessel usually dominated the plexus and generally, but not invariably, occupied a central position (fig. 1 *A, D* and *E*).

7. The manner in which the intraneural vascular pattern was established was fundamentally the same in the sciatic trunk and its medial and lateral popliteal branches, and the terminal capillary meshwork was, apart from minor variations, of approximately the same density in all situations.

However, the size, number, position and mode of branching of the intraneural arterioles were subject to such a considerable range of variation in different subjects, as well as at different levels in the same nerve, that no two patterns were alike in detail. There was certainly no pattern which was constant or characteristic for any section of the nerve. Moreover, the form taken by the pattern was quite unpredictable. The differences appeared to be due to minor variations in the pattern designed to provide the most effective blood supply to the nerve in terms of its anatomic structure. There was a suggestion that they were, to a large extent, determined by the number, size and site of entry into the nerve of the arteriae nervorum, by the fascicular pattern of the nerve and by its connective tissue framework; these are known to be variable morphologic features.

Though a comparison of the intraneural vascular pattern of two segments of the nerve will reveal obvious differences, the evidence suggests that there is nothing in those differences to indicate that one receives a better or a poorer blood supply than the other.

REGIONAL SOURCES OF SUPPLY

The source and number of the nutrient arteries are set out in tables 1 and 2. In 11 specimens the sciatic nerve divided high in the thigh or emerged from the pelvis in two divisions. The data on these specimens have been presented separately.

For the sake of convenience, no distinction has been drawn in the tables between nutrient arteries of the direct and those of the indirect type. Nutrient arteries included under the heading of muscular were traced into the nerve from fine muscular branches, the parent stem of which could not be ascertained with certainty.

GLUTEAL REGION

Nutrient arteries were traced intraneurally into the sciatic nerve from the sacral plexus. The origin of these vessels was not established.

Inferior Gluteal Artery.—The major supply to the nerve in the buttock was provided by the inferior gluteal artery (one to six branches), which supplied the nerve in all but 4 specimens.

On entering the buttock the inferior gluteal artery descended medial to the nerve. The nutrient arteries approached the nerve from the medial side and, after a course of variable length on the surface of the nerve, entered its inner margin, deep or superficial surface. Occasionally large branches of the gluteal artery crossed superficially or deep to the nerve in this situation and supplied it as they did so. It was unusual for a nutrient artery to approach and enter the nerve from the lateral aspect—when this occurred the twig was small and was derived from a muscular branch.

Hyrtl,[4] Henle,[5] Holl,[6] Quénu and Lejars[7] and Rauber[12] described a nutrient vessel from the inferior gluteal artery, and this is now universally recognized as the arteria comitans nervi ischiadici. Bartholdy[8] objected to this term on the grounds that this branch is a true nutrient artery and, moreover, is not the only nutrient twig supplied by the gluteal artery. He claimed that the inferior gluteal artery gave a branch to the nerve in the pelvis and two in the buttock, with an additional supply from the branches to

TABLE 1.—*Source and Number of Nutrient Arteries to the Sciatic Nerve in Man* *

Specimen No.	Buttock		Thigh		Popliteal Fossa										Leg				
					Medial Popliteal				Lateral Popliteal						Posterior Tibial			Anterior Tibial	Musculocutaneous
	Inf. Glut.	Cruc.	Perf.	Pop.	Perf.	Pop.	Gen.	Musc.	Perf.	Pop.	Gen.	Musc.	C. Fib.		Post Tib.	Peron.	Musc.	Ant. Tib.	Ant. Tib.-Peroneal
1 R	2	1	3	..	..	..	1	1	..	..	..	..	..		9	1	..	9	3
1 L	1	1	3	1	..	..	..	2	..	..	..	2	1		8	..	1	12	3
2 R	2	1	1	..	..	1	..	1	..	..	..	1	..		5	..	..	8	3
2 L	2	..	4	..	..	..	..	..	..	..	1	1	..		4	..	3	6	..
3 R	1	..	5	..	..	2	..	..	..	1	..	..	1		7	..	..	4	2
3 L	1	..	9	..	..	1	1	1	..	..	1	..	2		7	..	..	4	4
4 R	2	1	8	1	..	2	..	..	..	1	..	2	..		6	1	1	8	2
4 L	1	1	4	..	..	..	..	..	..	1	..	..	1		9	..	..	8	5
5 R	1	1	3	1	..	..	..	2	..	..	..	2	..		6	..	5	6	2
5 L	1	1	3	..	1	1	..	..	..	..	1	1	..		8	..	1	6	3
6 R	1	1	4	1	..	5	..	..	..	..	..	4	..		8	..	..	4	4
6 L	1	1	3	..	..	3	..	..	..	..	..	..	..		8	2	..	6	1
7 R	1	..	6	..	2	4	..	..	1	..	..	1	1		7	1	5	7	5
7 L	2	..	3	..	..	2	..	..	..	2	..	1	..		5	..	..	6	1
	1 Sup. glut.																		
8 R	2	1	7	..	..	2	..	..	..	2	..	..	..		6	3	1	7	1
8 L	2	2	8	1	..	1	..	..	..	1	..	2	..		8	..	7	7	2
9 R	1	1	4	..	..	3	..	..	..	..	..	..	..		5	..	..	6	4
9 L	1	1	6	..	..	2	..	..	..	2	..	..	2		6	1	1	7	3
10 R	2	1	6	..	1	1	..	..	1	1	..	..	..		9	..	..	5	1
10 L	1	2	6	..	..	4	..	..	3	..	..	..	..		4	..	2	5	1
11	1	2	2	1	..	..	1	..	..	..	1	..	..		2	..	..	2	..
12	3	3	8	..	..	1	..	..	..	1	..	..	1		3	1	4	4	..
13	2	1	2	..	..	1	..	1	..	..	..	1	..		4	..	2	6	..
14	1	..	4	..	..	3	..	..	..	1	..	..	1		3	..	2	2	2
15	1 Pud.	1	9	..	..	2	1	..	..	..	..	..	..		10	..	..	5	1
16	..	1	6	..	..	1	..	..	..	..	1	..	..		11	..	1	7	..
17	1	1	4	..	..	1	..	..	..	..	..	..	1		4	..	3	7	2
18	..	1	5	..	..	1	..	..	1	..	..	..	..		5	..	1	6	2
19	1	2	14	..	..	4	..	1	..	1	..	..	..		3	..	2	13	2

* In this table, and in table 2, C. Fib. indicates circumflex fibular artery; Cruc., crucial anastomosis; Gen., genicular arteries; Inf. glut., inferior gluteal artery; Musc., muscular branches; Perf., perforating system of arteries; Peron., peroneal artery; Post. tib., posterior tibial artery; Pop., popliteal artery; Pud., internal pudendal artery, and Sup. glut., superior gluteal artery.

TABLE 2.—*High Division of the Sciatic Nerve*

A. Buttock and Thigh

Specimen Number	Sciatic				Medial Popliteal			Lateral Popliteal		
					Buttock		Thigh	Buttock		Thigh
	Sup. Glut.	Inf. Glut.	Cruc.	Perf.	Inf. Glut.	Cruc.	Perf.	Inf. Glut.	Cruc.	Perf.
20 R	..	1	1	2	..	..	2	..	..	1
20 L	..	1	1	..	..	..	2	..	..	1
21 R	..	3	2	..	..	..	5	..	..	2
21 L	..	2	1	..	..	..	1	..	..	1
22	..	..	..	..	1	..	4	2	2	4
23	..	..	..	..	..	1	5	1 sup. glut.	..	5
24	..	..	..	..	3	..	7	3	..	4
25	..	..	..	..	2	1	9	1	..	6
26	..	..	..	..	1	1	1	1	1	1
27	1	1	..	..	..	1	3	..	2	1
28	..	..	..	..	1	3	2	1	3	2

B. Popliteal Fossa and Leg

Specimen No.	Medial Popliteal							Lateral Popliteal					
	Popliteal Fossa				Leg			Popliteal Fossa			Neck of Fibula	Leg	
	Pop.	Gen.	Musc.	Perf.	Post. Tib.	Peron.	Musc.	Pop.	Gen.	Musc.	C. Fib.	Anterior Tibial Ant. Tib.	Musculocutaneous Ant. Tib.-Peron.
20 R	1	1	..	..	5	..	2	..	1	3	1	15	4
20 L	1	..	..	..	5	..	..	..	1	..	1	5	1
21 R	1	..	..	..	3	5	..	..	1	..	1	5	3
21 L	1	2	..	..	9	2	..	..	..	..	..	7	2
22	1	..	..	..	8	..	2	..	..	3	1	9	1
23	4	..	..	..	5	..	1	..	..	..	1	6	1
24	1	..	..	..	2	..	2	..	..	..	1	5	2
25	2	..	2	..	7	..	..	1	..	1	..	4	3
26	..	..	1	..	2	1	1	..	..	..	1	9	..
27	2	..	..	..	4	..	..	..	1	..	..	3	..
28	1	..	1	..	4	4	..	..	..	1	1	5	4

muscles of the hip. According to Tonkoff,[9] this artery in most cases sends a twig to the nerve immediately it enters the buttock and another at the level of the ischial tuberosity, though on occasions he traced several (three to four) nutrient vessels of approximately the same caliber to the nerve. Haller [2] also described two nutrient arteries and Sappey [12] several nutrient arteries from this source, while Rauber [12] stated that muscular branches to the hamstring and adductor muscles provide nutrient vessels which accompany the nerve to the lower part of the thigh.

Crucial Anastomosis.—In the neighborhood of the quadrantus femoris muscle a supplementary and important supply (one to six nutrient arteries) was provided in most specimens by the arterial channels forming the crucial anastomosis. Owing to the dimensions of the anastomosis, it was not always possible to ascertain with accuracy the particular component from which the nutrient supply was obtained. On the evidence available, however, it was concluded that in the majority of the specimens the supply was provided by the medial femoral circumflex artery; the next most frequent source was the ascending branch of the first perforating artery, and only rarely did the supply come from the lateral femoral circumflex artery. The nutrient arteries from this system approached the nerve from its medial, lateral and deep aspects.

Henle [5] described a supply from the medial femoral circumflex artery but stated that the nutrient arteries recorded by other investigators as coming from the lateral femoral circumflex artery were not seen by him. Bartholdy [8] claimed that the nerve is frequently supplied by the medial femoral circumflex and only seldom from the lateral femoral circumflex artery. A supply from the medial femoral circumflex artery was recorded by Tonkoff [9] in 9 out of 10 specimens.

Superior Gluteal and Internal Pudendal Arteries.—Nutrient arteries were also observed coming from the superior gluteal and internal pudendal arteries, but reference to the tables will indicate the rarity of such a supply. Hyrtl [4] and Bartholdy [8] both recorded a supply from the latter artery.

THIGH

In the thigh the nerve was constantly vascularized by one or more of the perforating arteries or from the anastomotic chain which these vessels outline on the posterior surface of the adductor magnus muscle (fig. 2). Some of the largest nutrient arteries observed passing to the sciatic nerve were derived from this system. They varied from one to fourteen in number, and the direct type predominated. It was uncommon to see long stretches of the nerve in the thigh without an entering nutrient artery. No distinction has been drawn between the various perforating arteries, since none predominated in supplying the nerve and frequently the nutrient arteries were derived from the anastomotic chain outlined by them. The nutrient arteries from this system commonly approached the nerve from its anterolateral aspect, though occasionally large muscular branches perforated the nerve en route to their destination.

Fig. 2.—Illustration of a dissection, showing the blood supply to the sciatic nerve from the inferior gluteal artery, crucial anastomosis and, in particular, the perforating anastomotic chain. The nerve has been displaced medially to demonstrate the latter.

A supply from the perforating arteries was recorded by Hyrtl [4] (second or third), Henle,[5] Quénu and Lejars [7] and Bartholdy.[8] Tonkoff

described a constant nutrient artery from the first perforating artery by way of a muscular branch to, what he calls, the triceps muscle—in 6 out of his 10 specimens two nutrient arteries reached the nerve from this source. In only 2 of 10 specimens did he find the nerve receiving a supply from the second perforating artery.

POPLITEAL FOSSA

On entering the popliteal fossa the blood supply of the sciatic nerve or its popliteal branches was taken over by the popliteal artery and its branches. At the upper angle of the fossa they occasionally received a supply from the last perforating artery or from muscular branches of the femoral artery which had pierced the adductor magnus muscle. In the fossa the nutrient arteries may enter any aspect of the nerve or its divisions.

The medial popliteal nerve is intimately related to the popliteal artery, a fact which accounts for the high incidence of direct nutrient arteries from this source. Additional vessels were traced into the nerve from muscular and musculocutaneous branches of the popliteal artery and on occasion from the superior genicular system.

The lateral popliteal nerve, on the other hand, diverges from the artery as it descends to reach the neck of the fibula. For this reason its nutrient arteries were usually derived from more adjacent vessels, as represented by the muscular, cutaneous, musculocutaneous and superior lateral genicular branches of the popliteal artery. Failure of the nerve to establish a close relationship with a major arterial channel was also reflected in the large number of specimens in which no arteriae nervorum, or a single vessel only, reached the lateral popliteal nerve in the fossa.

Previous investigators have reported nutrient arteries reaching the popliteal nerves from the following sources: popliteal artery (Haller,[2] Walter,[3] Henle,[5] Bartholdy,[8] Tonkoff[9] and Portal[11]); medial and lateral sural and superior lateral genicular arteries (Hyrtl,[4] Bartholdy[8] and Tonkoff[9]); musculocutaneous branch of the popliteal and muscular branches from the femoral artery which had passed through the adductor magnus muscle (Tonkoff[9]).

Posterior Tibial Nerve.—In the posterior compartment of the leg the posterior tibial nerve and artery are closely bound together. It is therefore not surprising to find the nerve constantly receiving a large number (two to eleven) of small nutrient twigs directly and at frequent, though irregular, intervals along its course. An additional supply was provided by the peroneal artery and, indirectly, by the muscular branches of the two aforenamed vessels.

In the distal third of the leg it was by no means uncommon to see the tibial nerve perforated by the main arterial channel or one of its large branches (in 8 out of 40 specimens).

Tonkoff[9] alone has given a detailed account of the blood supply of this nerve. He stated that the nerve customarily receives a nutrient branch from the peroneal artery not far from its origin and four to five from the posterior tibial artery. When the latter artery was not developed, the nutrient twigs were said to come from the peroneal artery and its muscular branches. According to him, the number of nutrient arteries in the lower half of the leg exceeds that in the upper half, and this observation was confirmed in the present investigation. Bartholdy[8] found the nerve to be profusely supplied as far as the malleolus by the posterior tibial artery.

Lateral Popliteal Nerve.—At the point where the nerve is related to the neck of the fibula it was accompanied by the circumflex fibular artery, which frequently provided one or two arteriae nervorum in this situation—usually one entered the nerve where it was dividing into its superficial and deep divisions.

The musculocutaneous division was supplied in the interval between the peroneus muscles and the extensor digitorum longus muscle by large muscular arteries.

The anterior tibial nerve was supplied by the anterior tibial artery in the anterior compartment, where the intimacy of the neurovascular relationship was reflected in the large number (two to thirteen) of small nutrient arteries which the nerve received at frequent, but irregular, intervals. As in the case of the posterior tibial nerve, the majority of the nutrient vessels were of the direct type, though a large number of the indirect type were observed passing to the nerve in the following manner: As the artery descended, it usually gave off many transverse muscular branches to the extensor hallucis longus muscle. As these crossed the nerve transversely on their way to their destination (here the nerve is usually interposed between the muscle and the artery), they frequently gave a nutrient vessel to the nerve.

In the malleolar region the nerve was also occasionally supplied by the perforating peroneal artery (one nutrient in 1 specimen and two in another) and the anterior medial malleolar artery

(one branch in 2 specimens)—these are not listed in the tables.

A nutrient supply to the nerve in the region of the neck of the fibula has been described by Hyrtl [4] (fibularis branch of the anterior tibial artery) and Tonkoff [9] (ascending nutrient artery of the recurrent tibial artery). This would correspond to the supply which in the present investigation was observed coming from the circumflex fibular artery.

Bartholdy [8] reported indirect nutrient arteries to the superficial peroneal nerve from muscular branches of the anterior tibial artery, while a supply from this source to the anterior tibial nerve was mentioned by Haller,[2] Hyrtl [4] and Bartholdy.[8] A supply to the anterior tibial nerve from the anterior medial malleolar artery was reported by Bartholdy.[8]

SUMMARY

In this report on the blood supply of the sciatic nerve and its popliteal divisions, attention is directed in particular to the disposition of the fasciculi and related nutrient vessels of the lateral popliteal nerve at the neck of the fibula. The relative susceptibility of this nerve to pressure is discussed on the basis of these observations.

The topographic features of the blood supply to the sciatic nerve and its divisions in the buttock, thigh, popliteal fossa and leg are described in detail.

University of Melbourne.

STUDIES ON CEREBRAL EDEMA

II. REACTION OF THE BRAIN TO EXPOSURE TO AIR; PHYSIOLOGIC CHANGES

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Our previous studies have shown that when one area of the hemisphere of the cat brain has been exposed to the air for a few hours after the dura has been opened, an acute reaction takes place. It was found that although this reaction is more pronounced in the exposed area, more remote regions in both hemispheres, as well as the subcortical structures, are also affected.

The pathologic changes in the reaction of the brain tissue have been described.[1] In its earliest phases a vasodilatation takes place, which reaches its maximum about two hours after the beginning of the exposure; by that time the pulsations of the brain disappear, and a certain degree of cerebral swelling may be noticeable. Intravenous injection of trypan dyes given immediately after the exposure reveals an increase in the permeability of the blood-brain barrier, as shown by the diffuse staining of the brain with the trypan solutions, due to the leakage of the dye through the capillary endothelium into the intercellular spaces. Microscopic examination of the brain shows morphologic changes in the vessels; capillaries are collapsed and empty or dilated and engorged; some show aneurysm-like dilatations; others have their walls broken, and actual hemorrhages are seen. There is widespread diapedesis in both the gray and the white matter, and the perivascular spaces are distended. With the benzidine stain areas of ischemia are evident, being more marked in the exposed area than in the rest of the brain. Neuronal changes are seen very early, and they are characterized either by swelling, chromatolysis and liquefaction or shrinkage and homogenization with dilatation of the perineuronal spaces. Microglial cells show moderate and brief mobilization. After forty-eight hours, the histopathologic picture begins to return to normal, and at the end of the third or fourth day the preoperative picture is almost reestablished. We concluded that the whole picture could be considered as a mild, edema-like reaction due to a primary alteration, both functional and anatomic, of the integrity of the circulation, the cellular alterations being secondary to the circulatory changes.

In the present studies we shall describe some of the physiologic changes observed in our animals as the result of the exposure. They include changes in the electrical activity of the cortex, changes in the p_H of the exposed cortex and changes in permeability of the capillaries.

MATERIAL AND METHODS

Technic of Recording.—The technic [1] of the exposure has been given in detail in our previous paper. The present studies were also made on cats, a total of 40 animals being used. Electroencephalograms were taken before and at varying times, from five hours to thirteen days, after operation. Most of our electroencephalograms were taken with the animal under anesthesia induced with pentobarbital sodium. Others, however, were taken with the use of curare or on the unanesthetized animal. When the animal was anesthetized, three fourths of the full dose of the anesthetic was given intraperitoneally, and the electroencephalogram was recorded one and one-half hours later in order to obtain the greatest similarity in the records. The curare [2] was given intramuscularly, and records were taken once the maximum degree of paralysis was obtained.

The technic used with the unanesthetized animal was similar to the method described by Rheinberger and Jasper.[3] Fine silver electrodes, made of wire 0.5 mm. in diameter, were rounded to a small ball on one end by heating and were insulated, except for the extreme end, with rubber coating. Insertion of the electrodes was carried out with the cat under surgical pentobarbital sodium anesthesia and with strict aseptic precautions. After reflection of the skin and subcutaneous tissues, straight-sided burr holes (1.5 mm. in diameter) were made through the skull. Care was taken not to injure the dura. The rounded ends of the silver wires were inserted through the holes to the surface of the dura and secured with sterile wooden wedges, which were then cut flush with the surface of the skull. The electrodes were so placed that one overlay the frontal, the central and the occipital region each of both hemispheres. All wires were led posteriorly and fastened in one or more

From the Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute.

1. Prados, M.; Strowger, B., and Feindel, W.: Studies on Cerebral Edema: I. Reaction of the Brain to Air Exposure; Pathologic Changes, Arch. Neurol. & Psychiat. **54**:163 (Sept.) 1945.

2. A brand marketed by Burroughs Wellcome & Co., Inc., and Intocostrin (E. R. Squibb & Sons) were employed.

3. Rheinberger, M. B., and Jasper, H.: Electrical Activity of the Cerebral Cortex in the Unanesthetized Cat, Am. J. Physiol. **19**:186, 1937.

places to the muscle sheath, and the skin was then sutured. The cats did not show any disturbance from these attachments. The following day electroencephalograms were taken by soldering the ends of the silver wires to wire leads and connecting to the recording machine.

In the anesthetized or the curarized animal the electrodes were placed on the scalp. The head was shaved, and silver chloride–felt electrodes were fastened to the skin with collodion, contact being secured by means of electrode jelly. The electrodes were placed over the areas corresponding to the regions of the skull in which the electrodes were inserted in the unanesthetized animal, so that in all experiments we could compare the same cortical regions. The electrodes were connected to a four channel, ink-writer amplifier in such a manner that the central electrode of each side was shared in common with the frontal and the occipital electrode of the same side. The records were taken with the animal resting on a cushioned box in an electrically shielded, dark, sound-proofed room, with the recording system in an adjacent room.

Because of the individual differences of the electrical activity of the brain in our animals, preoperative records were taken in each experiment. Most of the preoperative records were taken one or more days preceding the operation; a few, however, were obtained immediately before the exposure. Sample elctroencephalographic tracings were taken at various gains so that direct comparison with the postoperative records at their optimum gain could be made. Postoperative records were taken on some animals on the second, fourth and sixth days after operation and on others on the first, third and fifth days. Some of the records were taken even on the seventh and ninth days; only 1 was taken on the thirteenth day after the exposure.

Studies of p_H.—Four acute experiments were carried out on cats in which the p_H of the exposed cortex was determined continuously over periods of four hours. The apparatus used was a modification of that previously described by Dusser de Barenne and associates. Glass electrodes filled with silver acetate were made according to the method described by Nims [4] and, with a silver chloride-saline solution wick electrode, were placed on the pial surface of the cortex and used in conjunction with a modified form of the microvoltmeter of Burr, Lane and Nims, a Leeds and Northrup Type K Potentiometer and a Leeds and Northrup Galvanometer No. 2420. The electrodes were calibrated immediately before each experiment against one-fifteenth molar phosphate buffer standard. Voltages were read off directly from the potentiometer at five to ten minute intervals during the exposure and changed to p_H readings with use of the calibration curve. The glass electrode leading to the microvoltmeter was shielded. The exposures were made in the usual manner employed with cats under pentobarbital sodium anesthesia, but with some care to maintain the temperature of the surroundings as constant as possible.

The anatomic position of the electrodes on the cortex in all cases was either the lateral gyrus or the middle suprasylvian gyrus. The direct current potential gradings were not recorded but may be neglected in an estimation of the p_H to 0.05 unit; and throughout any one experiment they were stable enough to admit more accurate measurement. Variations in temperature of the surface of the cortex would bring the total estimated experimental error for the p_H to 0.1. Only the shifts in p_H values which were greater than the experimental error are mentioned as significant.

Studies of Permeability.—Intravenous injections of solutions of trypan dyes were used to determine the degree of permeability of the capillary endothelium. Trypan red or trypan blue was used in a 1 per cent aqueous solution, of which 20 cc. was injected intravenously at the end of the exposure and on the following day. The animal was killed thirty-six hours after the exposure. In a series of animals, adrenal cortex extract was given intramuscularly in a dose of 1 to 2 cc. per kilogram of body weight. One injection was given one and one-half hours before opening the dura; a second injection, at the end of the exposure, after the wound was closed, and a third, twenty-four hours after the first, about four hours before killing the animal. In 2 animals the adrenal cortex extract was sprayed over the exposed cortex by means of an atomizer at one hour intervals during the exposure. In most of our experiments we used the commercial preparation of the Connaught Laboratories, Toronto. In others we used an extract specially prepared by the Frosst Laboratories, Montreal. We used also a preparation offered to us by Dr. Kendall. In another series of cats we injected preparations of the anterior lobe of the pituitary made under Dr. Collip's supervision in the Research Institute of Endocrinology, McGill University. We used two preparations. First, we employed a diluted extract, of which 10 cc. was injected intraperitoneally each day over a period of five to eight days before the exposure. In other experiments we injected a single dose two hours before the exposure. We also used a special concentrated extract prepared by Dr. A. H. Neufeld [5] in Dr. Collip's laboratories according to the technic published by him. After many trials, we found that the dose of 1 mg. per kilogram of body weight, injected subcutaneously the day before the exposure in two or three fractionated doses, was the most adequate.

For these two series of animals treated with glandular preparations, electroencephalograms were recorded in the usual manner except in the experiments with trypan dyes, in which no electrical activity was recorded.

RESULTS

Normal Electroencephalogram of the Cat.—Our records for the unanesthetized animal, as well as for the curarized cat, were similar to those described by Rheinberger and Jasper.[3] These records were characterized by waves of very low amplitude and high frequency followed by long or short periods of high amplitude and slow frequency. This type of electroencephalogram is very similar to that found for man during sleep. These bursts of high amplitude and slow frequency were more noticeable in the frontocentral regions than in the more posterior areas and possibly represented synchronized potentials originating in the motor cortex (figs. 2 to 7 inclusive).

For the anesthetized animal, with scalp electrodes, the type of electroencephalogram varied

4. Nims, L. F.: Glass Electrodes and Apparatus for Direct Readings of p_H in Vivo, Yale J. Biol. & Med. **10**:241, 1938.

5. Neufeld, A. H.: Preparation of the Pituitary Corticotrophic Hormone, Proc. Soc. Exper. Biol. & Med. **54**:90, 1943.

somewhat. It was characterized by bursts of potentials of an amplitude ranging from 10 to 20 microvolts and a frequency of 15 cycles per second. These bursts had a duration of two to three seconds and occurred every five to eight seconds. Between these bursts were seen slow waves of a much lower amplitude, with a frequency of 4 to 5 cycles per second, on which potentials of much higher frequency and lower amplitude were superimposed. As a rule these bursts were bisynchronous; that is, they occurred simultaneously in all leads in both hemispheres. Sometimes, however, one hemisphere showed them a few tenths of a second before they appeared on the opposite side. The records of the occipital regions consistently showed a lower amplitude than those of the frontoparietal region. A certain dominance of the right hemisphere over the left was frequently observed. The number of bursts per minute, as well as their amplitude, changed with the depth of the anesthesia.

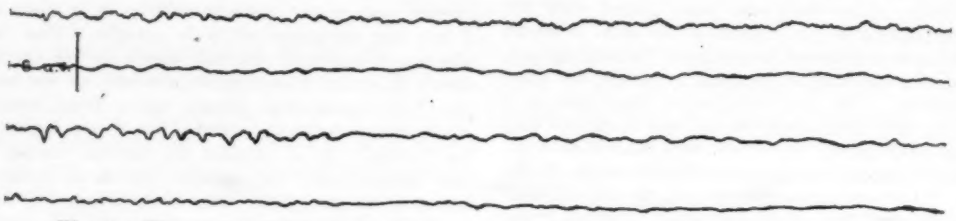

Fig. 1.—Electroencephalogram of the cat twenty-four hours after exposure. See text.

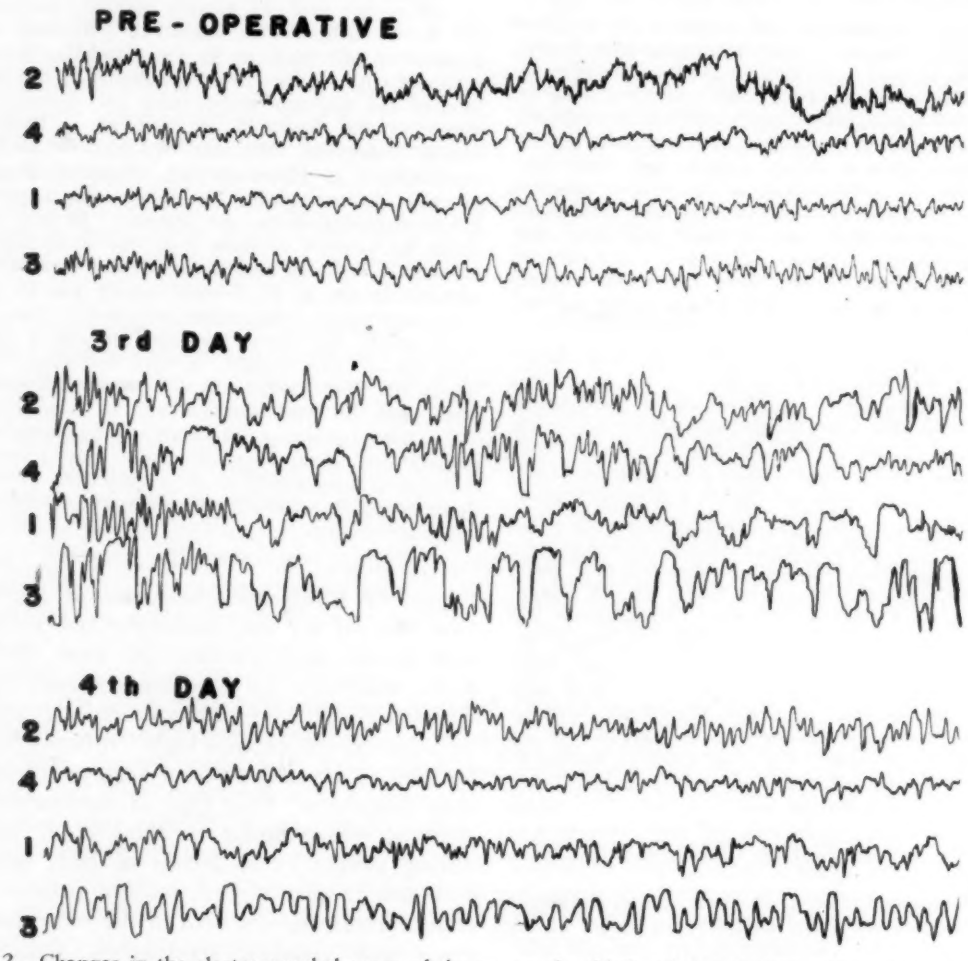

Fig. 2.—Changes in the electroencephalogram of the cat on the third and fourth days after exposure. Leads 2 and 4 are from the unexposed hemisphere; leads 1 and 3, from the exposed one.

Effect of Exposure on the Electroencephalogram. — The electroencephalogram recorded twenty-four hours after the exposure revealed a

considerable depression in the amplitude in all leads. The depression, which was always present at this time, varied somewhat from one experiment to another, and its picture differed in the unanesthetized animal, with dura leads, from that observed in the anesthetized cat, with scalp electrodes. With the latter the activity recorded in some cases was extremely low, and the record showed an almost flat line with random delta waves (fig. 1). With dura leads, however, the activity recorded consisted of extraordinarily fast waves of extremely low amplitude, although at times no activity at all was recorded. Occasionally, there were single bursts of potentials of higher amplitude and slow frequency.

On the third day the pattern of the electroencephalogram changed completely (fig. 2). There was a generalized increase in amplitude, which might be three or four times as great as that recorded before the operation. Sharp waves of a frequency of 6 to 7 cycles per second and slow waves of a frequency of 1½ to 3 cycles per second and an amplitude of 100 to 160 microvolts (scalp electrodes) were seen throughout the entire record, alternating at times with waves of much lower amplitude and frequency. Isolated typical spikes could also be seen, occasionally followed by one slow wave in a way identical with that observed during the epileptic discharge. With dura leads one found the same increase in amplitude, although here the difference between the postoperative and the preoperative record did not seem so dramatic. However, there was a definite increase in amplitude; the high ampli-

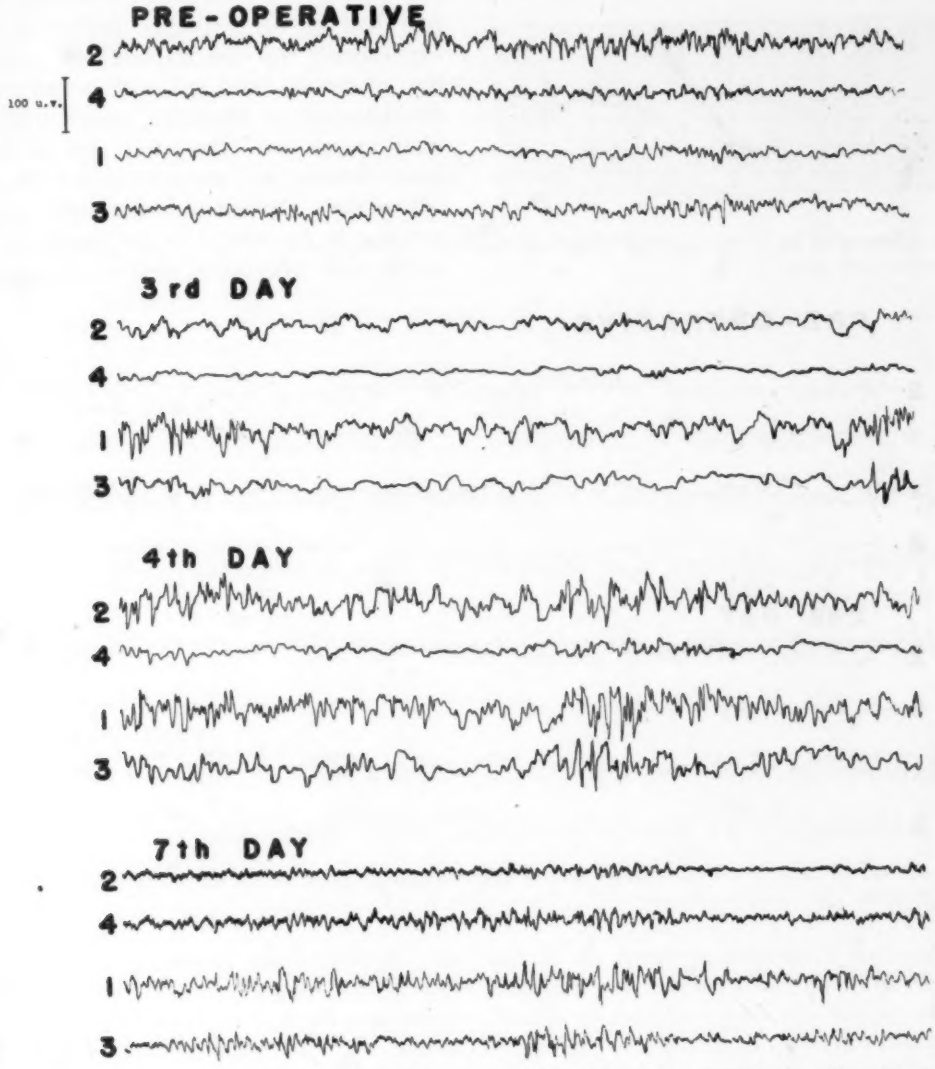

Fig. 3.—Return to normal of the electroencephalogram of the cat on the seventh day after exposure. Leads are as in figure 2.

tude and slow wave activity was not so marked and in some cases was seen only at random, and for many seconds only the high frequency activity might be recorded. Spikes were also seen.

The changes described could be seen in all leads, although the exposed side reacted more intensely than the unexposed one. We observed some correlation between the degree of swelling during the exposure and the intensity of these changes. Figures 2 and 3 show the electroencephalograms of 2 animals operated on at the same time. In 1 cat the swelling was extreme, and because of that the dura could not be closed. In this animal's record the changes are generalized and of the same type in all leads. In the case of the other animal, in which the swelling was not so marked, the picture is rather different. The parieto-occipital leads of both sides still show considerable depression, more pronounced, however, on the unexposed side. Random sharp waves can be seen in this lead, whereas in the exposed hemisphere the frontoparietal lead shows already the excitatory phenomena, but not so intensively as in the other animal.

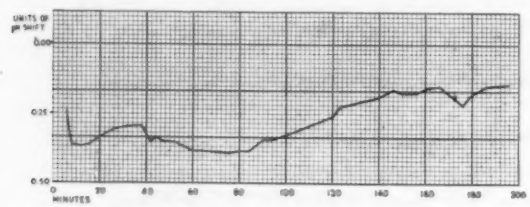

Fig. 4.—Changes in p_H of the cerebral cortex during the exposure. See text.

Between the fourth and the fifth day these electroencephalographic signs began to subside. The amplitude showed a tendency to come back to the preoperative condition; the spikes and sharp waves practically disappeared, although the delta activity might still persist. About the seventh or ninth day the electroencephalogram usually resembled the preoperative record.

Studies of the p_H.—Determinations of the p_H were carried out continuously over a period of four hours on the exposed cortex of 4 cats. The first half of the exposure period in 3 of our experiments was characterized by some fluctuation in the p_H level but with a definite shift in the direction of alkalinity, which might appear early or not until the latter part of the second hour. During the second half of the exposure our records showed a continuously progressive decrease in p_H values. In the fourth cat the shift to the acid side began almost immediately; but in this animal the recording was started some time after the actual operative exposure had been made, and there is no reason to believe it inconsistent with the other results. Figure 4 shows graphically the changes in 1 of our experiments, recorded over a period of two hundred minutes. After some fluctuations, lasting for fifty minutes, there was a definite, stable shift in the direction of alkalinity, which lasted less than half an hour. Eighty-five minutes after the beginning of the exposure one can see the continuously progressive shift to the acid side, as revealed by the decreasing p_H values.

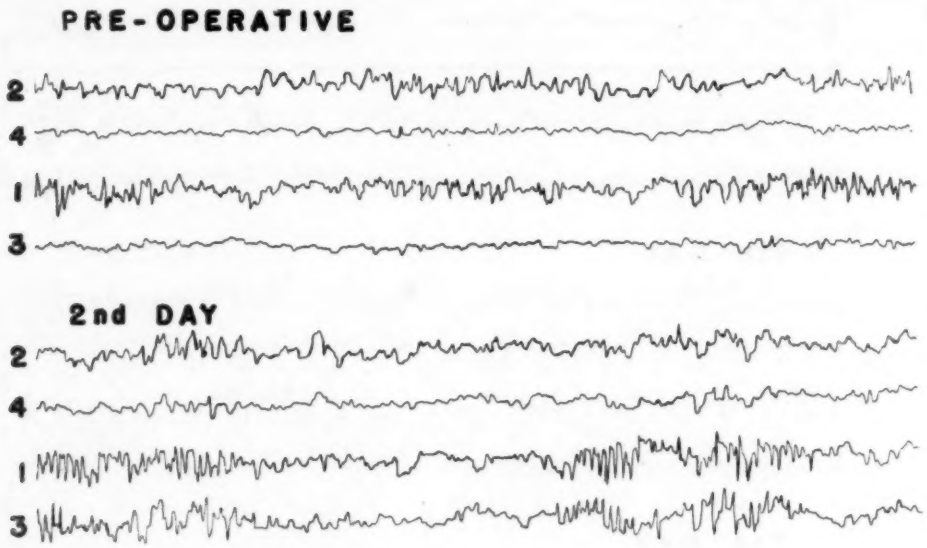

Fig. 5.—Effect of adrenal cortex extract on the electroencephalogram of the cat on the second day after exposure. See text.

Studies on Permeability.—Our previous studies showed that when solutions of trypan dye are

injected intravenously into the animal after the exposure, the whole brain is stained by the acid dye, but the exposed area more deeply than the rest of the brain. In other words, the exposure produces an opening of the blood-brain barrier which allows the leakage of the dye through the capillary endothelium. Our pathologic studies have shown, also, that the capillaries of the brain undergo changes which are responsible for the outflow of fluid into the intercellular spaces.

in this type of experiment. The upper record shows the electroencephalogram of the animal before the exposure, and the lower record, the electroencephalogram two days after the exposure. The changes present are mild. On the unexposed side one can hardly detect any change either in the amplitude or in the pattern of the electrical activity. The exposed hemisphere shows a moderate hypersynchrony, which is particularly noticeable in the central-posterior region, but the

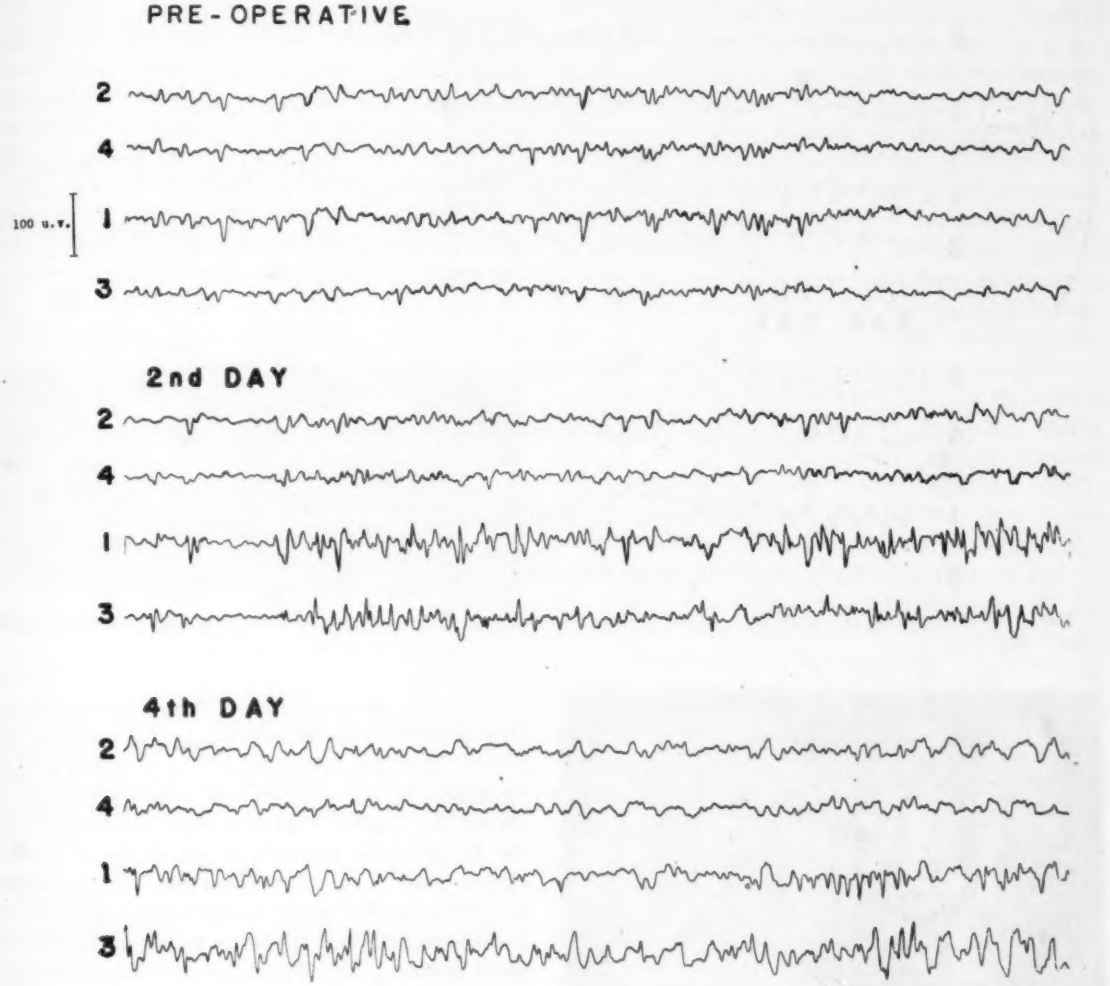

Fig. 6.—Effect of adrenal cortex extract on the electroencephalogram on the fourth day after exposure. See text.

We treated a series of animals before and after the exposure with injections of adrenal cortex extract and studied both the electroencephalographic changes and the behavior of the intravenously injected trypan solutions.

Effect of Adrenal Cortex Extract on the Electroencephalogram of the Exposed Brain: In a series of 10 cats we studied the effect of adrenal cortex extract on the electroencephalogram of the exposed brain. Figure 5 shows a typical record

increase in amplitude is low, the average amplitude being 80 microvolts, which represents an increase of only about 20 microvolts over that of the preoperative record. There are small numbers of single spikes or sharp waves.

In 2 animals the adrenal cortex extract was sprayed on the exposed area by means of an atomizer immediately after the opening of the dura and during the exposure. Electroencephalograms recorded on the second day after the ex-

posure showed only moderately increased amplitude in all leads of the exposed hemisphere; this increase in the record taken on the fourth day was practically limited to the posterior region of the same side (fig. 6).

In another series of 10 animals, we used a special preparation containing a high concentration of the corticotropic factor of the anterior lobe of the pituitary gland. The effect on the electroencephalogram was similar to that obtained when the adrenal cortex extract was employed. Figure 7 is the record of a typical experiment.

Effect of Adrenal Cortex Extract on Permeability of the Blood-Brain Barrier: Solutions of trypan blue were injected intravenously immediately after the end of the exposure into animals which previous to the operation had received adequate doses of adrenal cortex extract intramuscularly. Figure 8 shows the brains of 2 cats. In the case of the cat whose brain is shown in *A* the exposure was performed and the trypan blue injected but no adrenal cortex extract was given. The left hemisphere was exposed in both animals. In the case of the cat whose brain is shown in *B* the exposure was performed and the trypan blue injected in an identical manner except that 3 cc. of the adrenal cortex extract per kilogram of body weight was injected one and one-half hours previous to the exposure and three hours later. The control experiment (*A*) shows that the entire surface of the brain was tinged with the dye, although the staining was particularly intense in the exposed area of the left hemisphere. It can be noticed, also, that the exposed area is evidently swollen as compared with the rest of the brain, and the limits of the exposed area in the lateral and suprasylvian gyri can be detected by the degree of swelling. The surface of the brain in *B* shows a different picture. There is practically no staining at all with the trypan blue. Only in the posterior part of the lateral gyrus and a small patch in the posterior part of the suprasylvian gyrus can slight traces

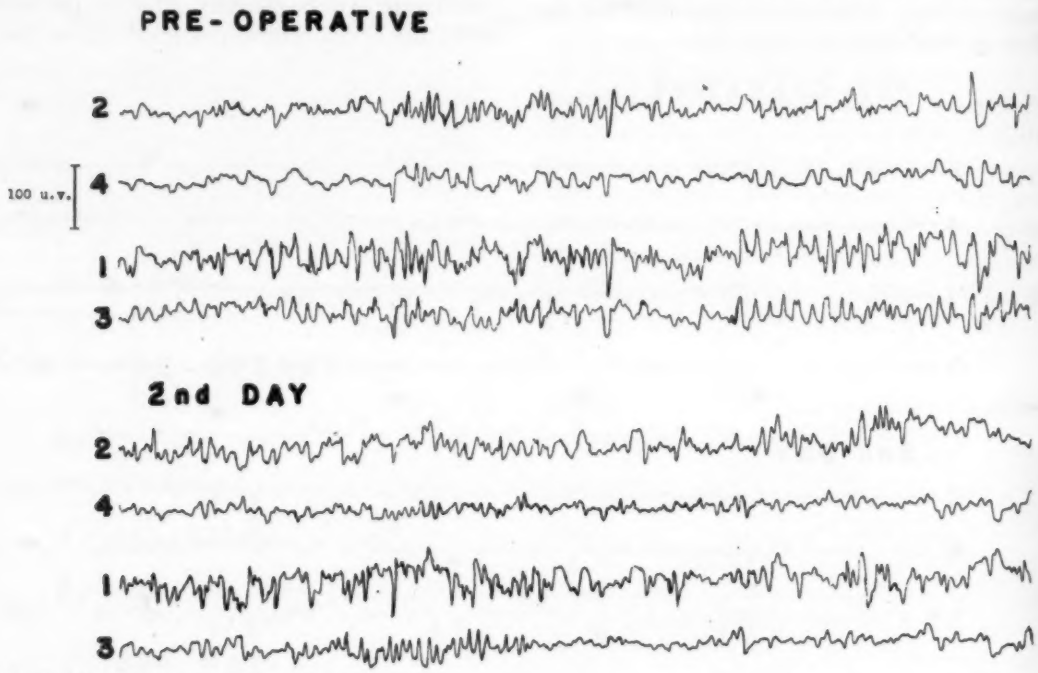

Fig. 7.—Effect of a preparation containing the corticotropic factor of the pituitary on the electroencephalogram. See text.

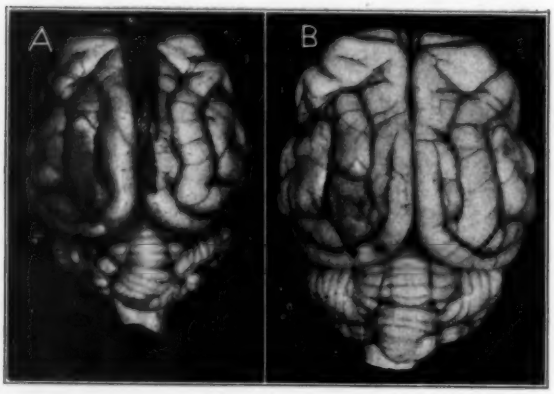

Fig. 8.—Brains of 2 cats in each of which the left hemisphere was exposed to the air for five hours and a solution of trypan blue was injected intravenously at the end of the exposure. In the cat whose brain is shown in *B*, adrenal cortex extract was injected intramuscularly during and after exposure. See text.

of the dye be seen. Moreover, no swelling of the exposed area can be seen at all. Figure 9 shows a coronal section of the brain of another animal. In *A*, which represents the control experiment, one can see that the cortex of the lateral gyrus is damaged as the result of the herniation of the brain substance through the wound in the bone, due to its swelling during the exposure. Of the cortical areas, the lateral and the suprasylvian gyrus, as well as the upper part of the sylvian gyrus, appear stained with the dye. The thalamus and other subcortical structures appear dark, especially when they are compared with the completely unstained section of the brain in *B*, which represents a section of the brain of the animal previously treated with the adrenal cortex extract.

The degree of efficiency of these glandular preparations in preventing the leakage of the dye through the wall of the vessels depends on the amount of the injected extract. We found the best responses in the cat when a dose of 2 cc. per kilogram of body weight was injected. This

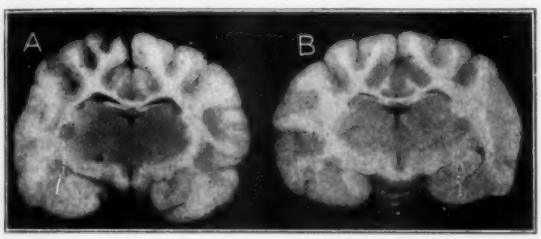

Fig. 9.—Coronal sections of the brains of 2 other cats, in an experiment similar to that illustrated in figure 8.

dose was repeated three, six and twenty-four hours after the exposure. An excessive dose seems to produce the opposite effect, especially when the preparation containing the corticotropic factor is used.

COMMENT

The type of electrical potentials described is characterized by a relatively short period of marked depression of the cortical activity (low amplitude waves; flat record with random slow waves) followed by a stage of hyperirritability, as indicated by the increase in amplitude of all types of waves and the hypersynchrony, represented by the presence of bursts of large slow waves and the sharp wave or spike and slow wave activity. This picture is almost similar to that described by investigators in cases of an acutely damaged cerebral tissue and is interpreted by Jasper and Penfield [6] as the expression of a metabolic deficiency associated with neuronal hyperirritability. The sequence and type of the electrical changes are almost similar, also, to those described by Sugar and Gerard [7] in conditions of acute cerebral ischemia in the cat. These investigators demonstrated that there exists a comparable sequence of phenomena between the clinical symptoms and the electroencephalographic signs. After the stopping of the circulation in the brains of cats due to occlusion of both vertebral and carotid arteries, they observed first increased respiration, followed by general tonic and clonic movements, and then progressively diminishing breathing and movements, ending in apnea and flaccid areflexia. The brain potentials showed, typically in the motor cortex and with special variations in other cerebral areas, a rather constant pattern. High frequency waves appeared or increased in speed and amplitude. In twelve seconds all fast waves, and in twenty seconds the slower ones, had disappeared. The record remained flat for the rest of a twenty second period of anemia. Five minutes after restoration of the blood flow, electrical activity was ushered in by low, irregular waves with a spindle of 6 to 9 per second, gradually fading into a newly starting spindle of considerable regularity; fast waves soon appeared, partly superimposed on other spindles; in four to six minutes the normal activity was reestablished.

These electroencephalographic changes following acute cessation and reestablishment of the blood flow may be compared with our observations, which differ only quantitatively from the experiments of Sugar and Gerard. The pathologic studies carried out on the brains of our animals showed a rather constant sequence of circulatory changes. In fact, after a period of several hours from the beginning of the exposure, characterized by definite vasodilatation, an ischemic condition occurred, more noticeable in the cortex, which was obvious in twenty-four hours, precisely when the brain potentials showed the fast, low amplitude activity or simply a flat line with some delta waves. This period of relative ischemia lasts generally no longer than twenty-four hours and is followed by a relatively slow but progressive reestablishment of the circulation, in some areas earlier than in others, the exposed area being always more affected than the unexposed area. It is not until four or five days later that the circulation becomes rather normal, although areas of impaired blood supply can still be seen. During these stages, the brain potentials show a generalized increased ampli-

6. Jasper, H., and Penfield, W. G.: Electroencephalograms in Post-Traumatic Epilepsy, Am. J. Psychiat. **100**:365, 1943.

7. Sugar, O., and Gerard, R. W.: Anoxia and Brain Potentials, J. Neurophysiol. **1**:558, 1938.

tude, with bursts of slow waves of still larger amplitude and random sharp waves and spikes; this hypersynchrony indicates a condition of hyperirritability of the neurons, with the tendency to discharge in unison. This hyperirritability disappears long before the delta activity, which may persist for many days.

That impaired cerebral blood supply may produce neuronal hyperirritability was suggested by Penfield [8] on the basis of his studies on the circulation in the brain of epileptic patients. Further electroencephalographic studies carried out by Jasper and Penfield [6] lend support to this conception by the recording of spikes and sharp waves from the border zones of the meningocerebral cicatrix and the evidence of cessation of the epileptic attacks after adequate surgical removal of the scar.

It is interesting, also, to mention that coincidental with the circulatory changes in the brains of our animals and the appearance of the cerebral potentials described there were neuronal alterations, mainly of two types; first, acute cellular swelling and chromatolysis with eventual liquefaction or simple appearance of "ghost" cells and, second, homogenization and shrinkage of the neurons. Of these two types, the first was the most commonly seen during the twenty-four hours following the exposure, whereas the second was predominant in the ensuing days. This observation makes possible the suggestion that probably there exists some correlation between the morphologic alterations in the neurons and the type of potentials observed.

The small series of studies on the p_H of the exposed cerebral area show that after a sudden and short shift in the direction of alkalinity of the brain a constant and progressive increase in acidity takes place, which is maintained during the entire time of exposure. We believe that the changes in the p_H values are related also to the sequence of vascular changes occurring in the cortex.

The importance of local cerebral blood flow in the maintenance of a constant physiologic p_H of the cortex has been demonstrated by Jasper and Erickson.[9] According to these investigators, an increase in blood flow produced by various means tends to increase the local p_H of the cortex. On the other hand, if the local blood flow does not increase after excessive neuronal activity, as in metrazol discharge, an acidity is produced which will persist somewhat longer than when the local vasodilator mechanism is more adequate. It would seem reasonable, also, that if the local flow is excessively decreased, as in congestion, and is insufficient to care for the normal resting activities of the neurons, a condition of local acidity might tend to result.

The shift toward alkalinity observed in 3 of our experiments would seem to be related to the hyperemia of the exposed cortex seen during the earlier part of the exposure, when one would expect an increase in blood flow in the exposed area. Since the p_H of arterial blood is usually somewhat greater than the local p_H of the cortex, this increased local blood flow would tend to increase the local cortical p_H. The progressive shift to the acid side which follows seems also to be due to the vascular conditions of the exposed area, since at this time congestion of the cortical vessels is evident and it would appear that the local blood flow is insufficient to maintain adequately even the resting activities of this area. The accumulation of metabolites accompanying this congestion would explain the decrease in the p_H of the cortex.

In our previous paper we have shown evidence that as a result of the exposure the capillary endothelium becomes more permeable. This allows not only an increased outflow of fluid into the interstitial spaces but the leakage of substances which in normal conditions are not permeable to the so-called blood-brain barrier. Our present studies show that adrenal cortex extract, either injected into the system or sprayed locally on the exposed cortex, has some protective effect on the brain potentials, preventing somewhat the depression of the first period and the subsequent excitatory phenomena. It also protects the capillary endothelium (if adequate doses of the extract are given) against the increased permeability which follows the exposure. This is demonstrated by the results of the trypan experiments, in which the brain remains unstained after the systemic injection of the dye solution.

At the present time considerable evidence indicates that the capillaries of the adrenalectomized animal are atonic, dilated and abnormally permeable. Menkin [10] showed that the leakage of trypan blue into extravascular spaces after the injection of leukotaxine could be reduced by either adrenal cortex extract or desoxycorticos-

8. Penfield, W. G.: Circulation of the Epileptic Brain, A. Research Nerv. & Ment. Dis., Proc. **18**: 605, 1938.

9. Jasper, H., and Erickson, T. C.: Cerebral Blood Flow and p_H in Excessive Cortical Discharge Induced by Metrazol and Cortical Stimulation, J. Neurophysiol. **5**:333, 1941.

10. Menkin, V.: Effect of Adrenal Cortical Extract on Capillary Permeability, Am. J. Physiol. **129**:691, 1940.

terone. Freed and Lindner [11] found that while cortex extract and corticosterone would prevent leakage of dye after injections of leukotaxine or peptone, desoxycorticosterone was without positive effect. Shleser and Freed [12] found that the adrenal cortex extract retarded leakage of dye from the capillaries after injections of peptone but that the corticosterone was ineffective. Cope [13] demonstrated that after administration of adrenal cortex extract there is a change in capillary permeability, permitting the retention of plasma protein within the blood stream.

In our experiments the circulatory changes, with the edema-like reaction, following exposure were pronounced in the region of the hypothalamus (fig. 10). This is not surprising when one remembers that this region is extraordinarily rich in blood vessels and that its capillaries are much more permeable than those in the rest of the encephalon.[14] The circulatory and vascular changes in this region produced by virtue of the exposure may depress to some extent the activity of the anterior lobe of the pituitary, owing to a certain damage of the nerve centers of the hypothalamus. This eventually impairs the release in sufficient quantity of the corticotropic hormone necessary to activate the adrenal cortex in the condition of stress involved in the operative procedure and the exposure. We suggest this as a possibility in view of the fact that in our animals previously treated with a corticotropic preparation the changes in the potentials were slight, although some hypersynchronism could still be seen in the exposed area on the third or fourth day after exposure. The permeability of the capillaries was also partly maintained.

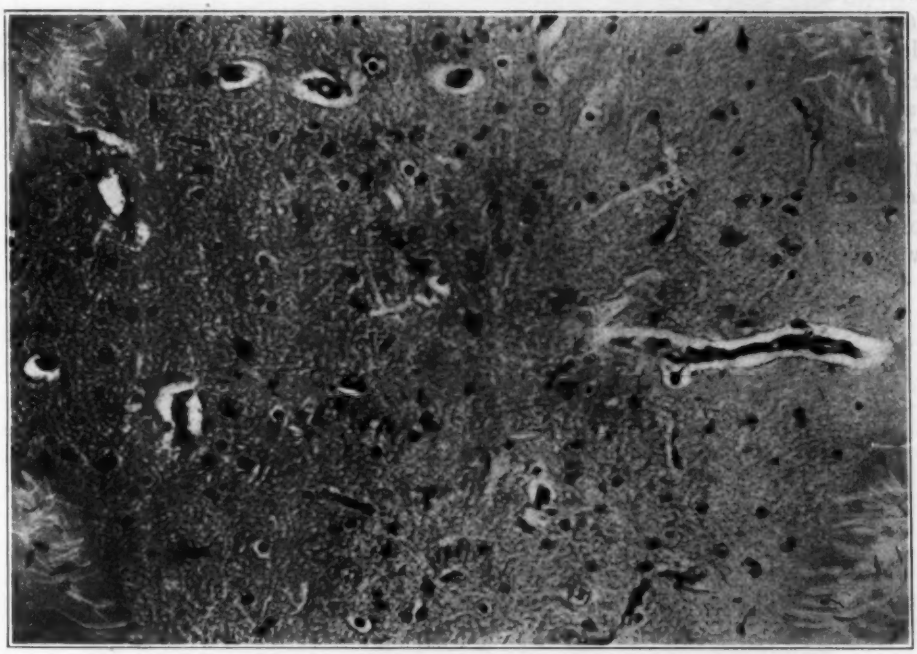

Fig. 10.—Edematous reaction of the hypothalamus of the cat twenty-four hours after the exposure.

The protective effects observed with the administration of adrenal cortex extract or a preparation containing the corticotropic factor of the anterior lobe could be explained either by the direct effect of the active principle of the adrenal cortex on the capillaries, which would keep their tonicity and permeability in good condition, or by the supposed beneficial action of the adrenal cortex extract in conditions of anoxia, as seems to have been demonstrated by various investigators.

In any case, we believe that the electrical changes described are due to an impairment in the metabolism of the brain tissue associated with hyperirritability of the neurons. The circulatory changes observed being primary to the electroencephalographic changes, we are inclined to accept the explanation that a condition of rela-

11. Freed, S. C., and Lindner, E.: The Effect of Steroids of the Adrenal Cortex and Ovary on Capillary Permeability, Am. J. Physiol. **134**:258, 1941.

12. Shleser, I. H., and Freed, S. C.: The Effect of Peptone on Capillary Permeability and Its Neutralization by Adrenal Cortical Extract, Am. J. Physiol. **137**:426, 1942.

13. Cope, O., cited by Swingle, W. W., and Remington, J. W.: The Role of the Adrenal Cortex in Physiological Process, Physiol. Rev. **24**:89, 1944.

14. Goldmann, E. E.: Vitalfärbung am Zentralnervensystem, Berlin, G. Reimer, 1913.

tive ischemia due to the transitory circulatory impairment accounts for the mechanism of the physiologic manifestations, as well as the pathologic picture observed as the result of the exposure.

Which factors determine these primary changes of the cerebral blood supply will need further investigations.

SUMMARY AND CONCLUSIONS

When one area of the cat brain has been exposed to the air for a few hours some physiologic alterations take place. They include changes in the electrical activity of the cerebral cortex, changes in the p_H of the exposed cerebral area and changes in the permeability of the capillary endothelium.

The electroencephalogram of the cat after the exposure shows a marked depression of the cortical activity, which lasts about twenty-four hours. This is followed by an excitatory state, characterized by a generalized increase in the amplitude and frequency of the cortical potentials and the presence of frequent bursts of large sharp and slow wave and spike activity. These excitatory phenomena slowly subside, and between the fifth and the seventh day the electroencephalogram returns to the preoperative condition.

The p_H of the exposed cortex fluctuates somewhat during the first half of the period of exposure, but with a definite shift in the direction of alkalinity. During the second half of the exposure there is a continuously progressive decrease in the p_H value.

Adrenal cortex extract and extracts of the anterior lobe of the pituitary containing the corticotropic factor protect the cortex against the electroencephalographic alterations elicited by the exposure. They also prevent the swelling of the brain and the changes in permeability of the cerebral capillaries which follow the exposure.

These physiologic changes are explained as the result of the described functional and morphologic changes in the cerebral circulation which take place from the beginning of the exposure.

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Obituaries

SMITH ELY JELLIFFE, M.D.
1866-1945

When Smith Ely Jelliffe died, on Sept. 25, 1945, American neurology and psychiatry lost a versatile and able exponent. His breadth of learning and culture and his enthusiasm for his life's work combined to form a well rounded scientist, an able medical editor and a teacher of distinction.

(Photographed by Blackstone Studios, 20 West Fifty-Seventh Street, New York)

SMITH ELY JELLIFFE, M.D.
1866-1945

Dr. Jelliffe was born in New York city on Oct. 27, 1866. Both his parents were school teachers, and his father was later principal of a public school in Brooklyn, where most of his early life was spent. He was graduated from public school and then attended the Brooklyn Polytechnic Institute, with the idea of becoming a civil engineer. This idea, however, did not long survive, for he soon learned that he hated mathematics. His main interest was in biology, especially botany, and it was only natural that he should drift toward medicine. In 1889 he was graduated from the College of Physicians and Surgeons, New York, where his knowledge of botany turned him first to pharmacology. After an internship at St. Mary's Hospital, Brooklyn, and a service as junior pathologist in the Methodist Episcopal Hospital, he spent a year abroad, more in sight-seeing than in study. In 1890 the "Brooklyn Eagle Almanac" published his first written article, "A List of Plants in Prospect Park." His interest in botany persisted in his early teaching of pharmacognosy and pharmacology at the College of Pharmacy and, later, at College of Physicians and Surgeons. He continued to write on these subjects up to 1904.

Jelliffe was never able to say what it was that led him into neurology and psychiatry. He started in general medical practice in New York,

doing part time work as sanitary inspector for the board of health, but he used to spend his summers working in hospitals. The summer of 1896 was undoubtedly the turning point of his career. That summer he went to the Binghamton State Hospital in his search for what he wanted to do. There he met the man who was to help him shape his life and start him on the work that was to be the main field of his future. Dr. William Alanson White was on the staff at Binghamton; there began the close friendship that was to last and grow until White's death, in 1937. They were of the same stuff, that pair: They thought alike; they worked alike; they played alike. Their intimacy was great, and each supplemented the other in all that he did. They formed an editorial team that had no equal in American medicine.

There is little doubt that it was White who led Jelliffe toward psychiatry, but it was characteristic of the man that he should have turned first to neurology. His botanical training forced him to learn fundamentals first, and fundamentals for him meant morphology; and it was but natural that he should seek first to learn neuroanatomy. Neuroanatomy became a hobby, and for long after he had turned completely to psychiatry and psychoanalysis, neuroanatomy remained a pastime for him.

The summer of 1897 saw Jelliffe at Bloomingdale Hospital and 1898 at Craig Colony. One year before his first neurologic publication, "Preliminary Note on the Cytology of the Brains of Some Amphibia; I. Necturus," appeared in the *Journal of Comparative Neurology*. From then on, pharmacology and botany quickly disappeared from his bibliography, to be gone completely by 1904. His first psychiatric writing was his translation, with White, of Dubois' "The Psychic Treatment of Nervous Disorders," in 1905. By 1913 psychoanalysis begins to creep into his bibliography, to take an even more important place from then on. In that year he and White started the *Psychoanalytic Review*. Up to 1939, when his health began to fail, his articles and books totaled 411 publications.

Jelliffe early entered the field of medical editing because he liked to write and wanted to increase his income. In 1900 he became editor of the *New York Medical News*, and in 1905, associate editor of the *New York Medical Journal*. His first appearance with the *Journal of Nervous and Mental Disease* was in 1902, when he started on his long service as managing editor, which lasted until his retirement, in 1944. In 1907 he and White started the "Nervous and Mental Disease Monograph" series, which has contributed so much to the furtherance of knowledge in this subject. In 1915 Jelliffe and White first published their now standard textbook, "Diseases of the Nervous System."

The *Journal of Nervous and Mental Disease* was Jelliffe's first love, and he clung to it longer than to any other. It was through this journal that he wielded his greatest influence. While many may have skipped hurriedly through the original articles, nobody missed a word of Jelliffe's book reviews. He did practically all of them himself, and there always were many, in an easy-flowing style that offered a fine judgment on the books he read. He spared no punches, and he spared no praise in the straightforward honesty of his criticisms. His enthusiastic advocacy of psychoanalysis, at a time when psychoanalysis had not yet been accorded the recognition it enjoys today, was motivated by that same intellectual honesty that was a basic part of his personality. Even in his later years, when he was too ill to work, his enthusiastic partisanship for what he believed to be true never flagged, as all of us who received his frequent letters well know.

Dr. Jelliffe belonged to many medical societies and held office in most of them. He served as president of the New York Neurological Society, the American Neurological Association, the New York Psychiatric Society, the American Psychopathological Society and the American Psychoanalytic Society. Dr. Jelliffe married Helena D. Leeming in 1894, and they had 5 children, of whom 4 survive. In 1917 he married Bee Dobson, who also survives.

Jelliffe was primarily a physician, an editor and a teacher. Those who worked with him have many pleasant memories of his friendship, his loyalty, his intellectual honesty and his fine, kindly sense of humor. At Jelliffe's jubilee celebration, in 1939, Dr. Adolf Meyer paid him this tribute in his own words: "He lives for all his worth and enjoys it with us."

L. CASAMAJOR, M.D.

OTTO SITTIG, M.U.Dr.

1886-1944 (?)

According to the "Information Bulletin of the Embassy of U.S.S.R." (May 1945), Otto Sittig, M.U.Dr., professor extraordinarius of neurology and psychiatry in Prague, was murdered by the Nazis in the Oswiecim camp.

Otto Sittig was born in 1886 in Prague, where he graduated in 1911. He was first associated with Prof. Alfred Přibram and later with Prof. Arnold Pick, whose work on aphasia was faithfully carried on by Sittig. Sittig was an excellent clinician, gifted with the greatest patience and critical judgment. Numerous publications on diseases of the central and the peripheral nervous system will remain as his contribution to the advance of neuropathology. He had an unusually fine knowledge of the neurologic literature and tried to do his share in establishing international relations by translating the writings of English authors, among others the work of Hughlings Jackson, into the German language.

Rudolf Altschul.

Abstracts from Current Literature

Anatomy and Embryology

THE COURSE OF THE STRIAE MEDULLARES IN THE HUMAN BRAIN. THOMAS H. ALPHIN and WILLIAM T. BARNES, J. Comp. Neurol. **80**:65 (Feb.) 1944.

Alphin and Barnes studied the course of the striae medullares in the brain of an adult white man. The brain had been sectioned serially at 40 microns and stained by the Weil method for myelin. Owing to a somewhat unusual plane of section, which nearly paralleled the course of the striae medullares, it was possible to trace the course of the fiber bundles for a considerable distance. The striae medullares formed a prominent bundle of myelinated fibers on the floor of the fourth ventricle. When traced laterad, the bundle separated into three groups of fibers. The most rostral group, consisting of a small number of fibers, passed directly into the white matter of the cerebellum, which formed the lateral wall of the fourth ventricle at that point. More caudad a few fibers passed into the peduncle of the flocculus. Still farther caudad the majority of the fibers passed ventrad and entered the pontobulbar body external to the restiform body. When the striae medullares were traced medially, they were seen to dip into the medial raphe and, after a complete or partial decussation, to continue ventrally into the region of the arcuate nuclei. They could not be traced farther because of intermingling with ventral external arcuate fibers. Alphin and Barnes suggest that if the external arcuate nuclei be considered as caudally displaced pontile nuclei, the striae medullares would be analogous to the transverse pontile fibers. There is no evidence, however, as to which direction the fibers take. The authors emphasize that the fibers of the striae medullares are not auditory in function.

ADDISON, Philadelphia.

AN EXPERIMENTAL INVESTIGATION OF THE CONNECTIONS BETWEEN THE CORPUS STRIATUM AND SUBSTANTIA NIGRA IN THE CAT. HAROLD ROSEGAY, J. Comp. Neurol. **80**:293 (June) 1944.

Rosegay studied the reciprocal relations of the corpus striatum and the substantia nigra in the brains of 16 cats after experimental injuries. In 6 brains the substantia nigra was destroyed, and in 8 the head of the caudate nucleus was removed or damaged. The animals were allowed to survive for about two weeks after operation. The brains with lesions of the substantia nigra were prepared by the Marchi method for staining degenerating myelin. From the brains with lesions in the caudate nucleus selected sections were stained with cresyl violet to show retrograde cell changes. In addition, 2 brains were used for comparison, 1 from an animal subjected to frontal lobectomy and the other from an animal with a chronic lesion of the substantia nigra. Short protocols are given of the 14 main experiments. Rosegay found that lesions of the head of the caudate nucleus and of the anterior limb of the internal capsule gave rise to retrograde chromatolysis of the pars reticulata and the pars compacta of the substantia nigra. His experiments do not support the idea that the pallidum is a more important terminus than the striatum for efferent fibers from the substantia nigra. The present study suggests that the principal efferent connection of the substantia nigra is with the neostriatum. Thus, in addition to the strionigral and the pallidonigral connections, there are important connections in the reverse direction, viz., the nigrostriatal and the nigropallidal.

ADDISON, Philadelphia.

PHYSIOLOGIC EFFECTS OF BILATERAL SIMULTANEOUS FRONTAL LESIONS IN THE PRIMATE. FRED A. METTLER, J. Comp. Neurol. **81**:105 (Oct.) 1944.

Mettler observed the effects on 12 monkeys of making bilateral simultaneous lesions of varying extent on the frontal lobes and subsequently studied the exact extent of the lesions and their histologic consequences. He had previously studied the effects of unilateral lesions on the hemisphere, and in the present investigation he found that simultaneous removal of subareas of the frontal cerebral cortex may produce a result which is not only quantitatively but qualitatively different from the effect of unilateral operation on the same area. Also, the effects of operations done on the two hemispheres on the same day may be different from the effects produced by allowing an interval of time to elapse between the operations on the two sides. Bilateral simultaneous removal of area 4 immediately produces marked stiffness and resistance to passive movement, and these effects are essentially related to the ablation of that part of area 4 variously known as the suppressor area, the strip region or area 4 S. There is an immediate loss of adult locomotion and manual feeding patterns, and the animal is unable to chew and can only suck its food. Fine digital movements are acutely abolished and chronically impaired. The plantar response becomes difficult to elicit, and the threshold of the patellar reflex is raised. Section of the dorsal columns only slightly ameliorates the resistance produced by removal of area 4 and still further degrades the quality of the motor performance. Another effect noted was that the animals bilaterally deprived of area 4 cortex become abnormally sensitive to the effects of section of the vestibular nerve. Unilateral section of the vestibular nerve in such animals induces a reaction reminiscent of what is seen in carnivora, viz., rolling and fixation of posture.

ADDISON, Philadelphia.

THE DISTRIBUTION OF MYELINATED AFFERENT FIBERS IN THE BRANCHES OF THE CAT'S FACIAL NERVE. S. R. BRUESCH, J. Comp. Neurol. **81**:169 (Oct.) 1944.

To determine the number of myelinated fibers having origin in the geniculate ganglion, Bruesch transected the left seventh nerve 5 to 10 mm. distal to the stylomastoid foramen, just before it divides into its branches to the mimetic musculature. After a lapse of twelve to fourteen days the geniculate ganglia of both sides were removed and serial sections stained with thionine. Counts were made of the total number of cells and of the cells showing chromatolysis. On the right, intact, side, 4.2 per cent of the cells showed some degree of chromatolysis and on the side of operation, 12.4 per cent were so affected. The difference of 8.2 per cent is considered due to the transection. The total average count of cells in the geniculate ganglion was 1,711, and

8.2 per cent of this is 140, the average number showing chromatolysis. The inference is that there are 140 afferent fibers of geniculate ganglion origin in the motor nerves to the mimetic muscles. By gold chloride methods for nerve endings, Bruesch sought the receptors in the muscles connected with these afferent nerves. The only sensory nerve endings appeared to be free terminations in the adventitia of blood vessels in the muscles. Bruesch is inclined to regard these endings as connected with pain fibers. Also, fiber degeneration experiments were made to see how many afferent fibers from the mimetic muscles were tributary to the auricular nerve of the vagus. The facial nerve trunk was severed proximal to the union of the auricular nerve with the facial trunk. The number of myelinated nerves persisting in the peripheral facial nerve trunk twenty-one to thirty-six days after operation averaged 93. There are thus afferent fibers of both facial nerve and vagus nerve origin in the muscular branches of the facial muscles. As no proprioceptors were discovered in the muscles, these fibers are probably pain fibers. Bruesch considers this anatomic evidence to support the clinical views as to the existence of neuralgias of both geniculate ganglion and vagus nerve origin.

ADDISON, Philadelphia.

STUDIES ON THE NEUROMOTOR SYSTEMS OF STYLONYCHIA PUSTULATA AND STYLONYCHIA MYTILUS. YUEH-TSENG CHEN, J. Morphol. **75**:335 (Nov.) 1944.

Both the hypotrichous ciliates (Stylonychia pustulata and Stylonychia mytilus) possess a neuromotor apparatus. The neuromotor systems of these two species are similar. Each system consists of membranelles and their associated fibrils, undulating membrane and its basal fibril, dorsal cystostomal fibrils, ventral cystostomal fibrils, postesophageal fibrils, and anal, caudal and marginal cirri. The frontal cirri and the ventral cirri do not appear to be connected with the neuromotor system.

In S. pustulata, the five anal cirri are each supplied with a longitudinal fibril, while, in addition, one to three anal cirri each, has a transverse fibril. In S. mytilus, each of the five anal cirri is supplied with a bundle of five to eight longitudinal fibrils, but no transverse fibrils have been found. Each of the three caudal cirri is supplied with a single fibril in S. pustulata, and with a bundle of fibrils in S. mytilus. A single fibril connects the marginal cirri near the base. Each marginal cirrus has a terminal fibril running inward toward the central part of the body.

A deeply stained (hematoxylin) mass near the posterior end of the adoral band of membranelles in S. pustulata may be the neuromotorium. The silver impregnation technic did not reveal any silver line system.

REID, Boston.

Physiology and Biochemistry

EFFECT OF ANOXIA ON THE VESTIBULAR APPARATUS. A. POPOV and I. BORSHCHEVSKI, Am. Rev. Soviet Med. **1**:310 (April) 1944.

Popov and Borshchevski studied the effect of hypoxemia on 31 persons who were subjected to rocking on a four pole swing or placed in a low pressure chamber. Sixty-two experiments were performed on subjects while rocking in the swing under normal breathing conditions and while breathing a mixture with a lowered content of oxygen (8 to 12 per cent). The breathing mixtures were inhaled through a special mask. The rarefied mixture was inspired as the subject was moved in the Bárány chair and then subjected to the oxygen respiration test. He was then transferred to the four pole swing for fifteen minutes' rocking. This was followed by the oxygen respiration test after which the mask was removed, and normal respiration ensued. The data show that in some persons pallor, vertigo, blackout, sweating, cyanosis, nausea and vomiting were more pronounced under conditions of rocking and hypoxemia.

Two other series of experiments were undertaken in an effort to study the effect of altered barometric pressure on nystagmus. The results were uninformative, and the authors concluded that more sensitive methods of investigation must be devised.

GUTTMAN, Philadelphia.

PYRIDOXINE DEFICIENCY IN SWINE, WITH PARTICULAR REFERENCE TO ANEMIA, EPILEPTIFORM CONVULSIONS AND FATTY LIVER. MAXWELL M. WINTROBE, RICHARD H. FOLLIS JR., MITCHELL H. MILLER, HAROLD J. STEIN, RAUL ALCAYAGA, STEWART HUMPHREYS, ADOLPH SUKSTA and GEORGE E. CARTWRIGHT, Bull. Johns Hopkins Hosp. **72**:1 (Jan.) 1943.

Pigs, about 3 weeks old, were fed only crystalline vitamins, in addition to a basal diet. Microcytic anemia developed in from three to fifteen weeks in all the animals which received all the crystalline vitamins but pyridoxine hydrochloride. It was noted that the anemia which developed in pigs not given calcium pantothenate or choline chloride, in addition to the deprivation of pyridoxine hydrochloride, was similar in all respects to that observed in pigs lacking only the pyridoxine. A sharp increase in the reticulocyte count followed the administration of pyridoxine hydrochloride. These reached a peak on the second to the sixth day after administration of the first dose of pyridoxine. The increase affected particularly the hemoglobin and the volume of packed red cells, as well as the size of the corpuscles. The highest increase in the reticulocyte count, in the hemoglobin concentration and in the volume of packed red cells was observed when the anemia was most pronounced and large amounts of pyridoxine hydrochloride were given intravenously. Pronounced and uniform changes were observed in the spleen, liver and bone marrow of the animals in which pyridoxine anemia developed. The changes related to the presence of anemia were hemosiderosis in the spleen, liver and bone marrow and hyperplasia of the bone marrow. Mobilization of iron from the tissues and its utilization in blood formation are indicated by the disappearance of hemosiderosis and a fall in the iron content of serum following treatment with pyridoxine. Pathologic changes in the liver consisted of fatty infiltration and could be seen as vacuoles in the cells of the central portions of the hepatic lobules. The observations indicate that fatty infiltration of the liver occurs when either pyridoxine or choline or both are not furnished as supplements to the diet. Convulsions were observed in 20 of 26 pigs not given a supplement of pyridoxine hydrochloride, as well as in 6 of 16 pigs fed fractions of liver poor in pyridoxine. There was no consistent relationship between the time of onset of convulsions and the time at which significant anemia appeared. The convulsions ceased promptly after the administration of pyridoxine hydrochloride in the doses used in the treatment of the anemia. No changes in the brain were noted in any of the pyridoxine-deficient animals except in the lower portion of the medulla,

where fibers in the ascending sensory tract had lost their myelin sheaths. The changes were interpretated as being part of the degeneration of sensory neurons resulting from pyridoxine deficiency. The nature of the mechanism by which pyridoxine deficiency arrests the synthesis of hemoglobin and elevates the iron content of the serum is not understood.

PRICE, Philadelphia.

DETERMINATION OF CARBONIC ANHYDRASE IN HUMAN AUTOPSY TISSUE. W. ASHBY and D. V. CHAN, J. Biol. Chem. **151**:515, 1943.

In 1932 Meldrum and Roughton isolated from mammalian red blood cells a highly active enzyme which they called carbonic anhydrase. This enzyme catalyzes the reaction $H_2CO_3 \rightleftarrows CO_2 + H_2O$ and is responsible for the accelerated excretion of carbon dioxide from the blood. In any assay of the enzyme in tissues the presence of blood has presented difficulties. In this report a new adaptation of a method for measuring the blood content of tissues is described. The reproducibility of the technic is illustrated by complete determinations on adjacent portions of the central nervous tissue which indicate an average difference of 5 per cent.

PAGE, Cleveland.

OXIDATION OF FRUCTOSE BY BRAIN IN VITRO. J. R. KLEIN, J. Biol. Chem. **153**:295, 1944.

Fructose does not maintain the electrical activity of the cerebral cortex in the hepatectomized animal. However, whole brain and cortex oxidize fructose in vitro. These facts may be explained by assuming that the brain cells are impermeable to fructose in vivo or that the oxidation of fructose is not concerned in the maintenance of cortical activity. The latter supposition makes it necessary to assume that the metabolism of fructose by brain differs from the metabolism of dextrose, since the latter does support cortical activity in the hepatectomized animal. In the present work, the oxidation of fructose by brain preparations was studied in vitro. The data obtained indicate that the oxidation of fructose by brain in vitro follows the same pattern as the oxidation of dextrose. Thus, the data support the hypothesis that brain cells are impermeable to fructose in vivo.

PAGE, Cleveland.

WATER, NITROGEN, AND ELECTROLYTE CONCENTRATION IN BRAIN. L. EICHELBERGER and R. B. RICHTER, J. Biol. Chem. **154**:21, 1944.

Procedures are described by Eichelberger and Richter for water and electrolyte analyses of the cerebral hemispheres and the cerebellum. Total water, nitrogen and electrolyte concentrations were determined in brain, which was removed by bilateral craniotomy from normal dogs. For analyses the brain was separated into the cerebral hemispheres and the cerebellum with the brain stem. Analyses of the right and left hemispheres from the same animal gave the same values. The mean average results for the hemispheres expressed as units per kilogram of hemisphere, are as follows: total water 761.3 Gm., $\sigma \pm 8.3$; chloride 36.71 millimols, $\sigma \pm 1.05$; sodium 51.0 millimols, $\sigma \pm 2.4$; potassium 95.6 millimols, $\sigma \pm 4.7$; calcium 1.07 millimols, $\sigma \pm 0.07$; magnesium 5.63 millimols, $\sigma \pm 0.56$, and total nitrogen 18.9 Gm., $\sigma \pm 0.3$. The cerebellum with the brain stem gave the following mean average results: total water 745.0 Gm., $\sigma \pm 7.0$; chloride 35.19 millimols, $\sigma \pm 0.89$; sodium 50.8 millimols, $\sigma \pm 1.7$; potassium 92.7 millimols, $\sigma \pm 4.0$; calcium 1.07 millimols, $\sigma \pm 0.07$; magnesium 5.40 millimols, $\sigma \pm 0.30$, and total nitrogen 19.1 Gm., $\sigma \pm 0.5$. Because the analyses of the hemispheres and the cerebellum following extraction of the dried tissue with ether and petroleum ether gave low concentrations of chloride, sodium and potassium, the analytic results were not expressed in terms of fat-free tissue. The analytic results are of value for further experimental work on brain as control data, since it is impractical to take control brain tissue from the experimental animal.

PAGE, Cleveland.

PIAL CIRCULATION AND SPREADING DEPRESSION OR ACTIVITY IN THE CEREBRAL CORTEX. A. A. P. LEAO, J. Neurophysiol. **7**:391 (Nov.) 1944.

Leao observed the pial vessels of rabbits under dial anesthesia by means of a compound microscope and studied the variations in their caliber before, during and after the appearance of depression of the electrical activity resulting from electrical stimulation of the cortex. He observed a wave of marked dilatation of the pial vessels and increased blood flow traveling over the cerebral hemisphere concomitantly with the wave of depression in the electrical activity. Arteries increased in size from 50 to 100 per cent, and the veins became as scarlet as the arteries. The presence or absence of convulsive activity had no correlative variation with the degree of vascular change. Leao concluded that the vascular response was secondary to a local change in the activity of the nerve elements and that the increase in blood flow probably influenced in turn the activity of the cortical neurons.

FORSTER, Philadelphia.

MIDBRAIN AUDITORY MECHANISMS IN CATS. H. W. ADES, J. Neurophysiol. **7**:415 (Nov.) 1944.

Ades recorded from a cathode ray oscillograph the responses to sound stimuli from various parts of the midbrain of the cat. He found that the contribution of discharge through the inferior collicular commissure was negligible in the total activity of the inferior colliculus. The contribution of the contralateral ear to collicular response was found to be slightly greater than that of the homolateral ear. The functional bilateral equality in auditory conduction from the ears is probably due to bilateral terminations of secondary auditory fibers in the superior olivary nucleus. Significant numbers of fibers from the lateral lemniscus by-pass without synapsing in the inferior colliculus. The inferior colliculus was found to discharge through the superior colliculus, and it is considered an important reflex center for auditory integration.

FORSTER, Philadelphia.

RECOVERY OF FIBRE NUMBERS AND DIAMETERS IN THE REGENERATION OF PERIPHERAL NERVES. E. GUTMANN and F. K. SANDERS, J. Physiol. **101**:489, 1943.

Gutmann and Sanders studied the effect of crushing, cutting, suturing and nerve grafting on the number and size of the nerve fibers in the peripheral and the central stumps of the severed nerves and in the various nerve grafts. After the nerve was crushed or cut, the central stump regularly exhibited a decrease in size of all its constituent fibers, an observation suggesting that the outgrowth from the central stump is really an outflow of protoplasm from the neurons.

After the crushing, the peripheral stump was completely reconstituted with respect to both the number

and the size of fibers within two hundred and fifty to three hundred days. After the suturing or grafting, the peripheral stump of the regenerating nerve showed a deficit in number and in average size of the fibers even three hundred and sixty-four days after operation. No such nerve was observed ever to recover fully with respect to number or to size of fibers. There was a deficit particularly in the number of large fibers. The deficit in number of fibers in the peripheral stump was particularly noticeable below alcohol-fixed grafts, in which the number attained was only 60 per cent of the number present in the central stump. In such instances recovery of function was incomplete.

THOMAS, Philadelphia.

EXPERIMENTAL EDEMA OF THE BRAIN: IV. CEREBRAL CIRCULATION. S. OBRADOR ALCALDE and J. PI-SUÑER, Bol. d. Lab. de estud. med. y biol. **1**:99 (June) 1942.

The difference in oxygen content between arterial and venous blood was studied in adult dogs in which experimental edema of the brain had been produced by lesions in the region of the fourth ventricle. Simultaneous specimens of blood were taken from the femoral artery and the external jugular vein ten and fifteen to twenty minutes after the lesions were made in the fourth ventricle. The cerebral circulation was studied in this way in 8 animals. In 5 of them there was no significant change in the difference in oxygen content between venous and arterial blood. In 3 dogs there was a diminution of this difference, indicating a sudden increase in blood flow. Although the data are not conclusive, the authors indicate that in some cases an increase in circulation may be a factor in accounting for the appearance of edema of the brain.

SAVITSKY, New York.

Psychiatry and Psychopathology

CONVULSIVE SHOCK THERAPY IN INVOLUTIONAL STATES AFTER COMPLETE FAILURE WITH PREVIOUS ESTROGENIC TREATMENT. A. E. BENNETT and C. B. WILBUR, Am. J. M. Sc. **208**:170 (Aug.) 1944.

Bennett and Wilbur reviewed the records of 500 cases of psychoses and psychoneuroses occurring in women between the ages of 31 and 65 years. Seventy-five of the patients had received estrogens as therapy for the mental disorder. The condition of 41 was classified as involutional melancholia. Of the 75 patients, 64 received some form of shock therapy, but for 11 psychotherapy alone sufficed. A course of from six to eight shock treatments was given over a period of two to three weeks. After active shock treatment, patients remained in the hospital from ten days to two weeks for reeducative psychotherapy. The authors concluded that estrogens were of no value in the treatment of psychiatric disorders except for symptomatic relief of vasomotor symptoms.

MICHAELS, M. C., A. U. S.

RESPONSES OF SCHIZOPHRENIC PATIENTS TO INDUCED ANOXIA. W. CORWIN and S. M. HORVATH, J. Nerv. & Ment. Dis. **99**:149 (Feb.) 1944.

The impetus to studies of the effects on the human organism of exposure to environments containing low percentages of oxygen has come both from the field of high altitude aviation and from the various shock therapies of psychoses. To study these effects, Corwin and Horvath subjected 10 male schizophrenic patients to atmospheres containing, respectively, 14.6, 5.2 and 4.2 per cent of oxygen. The neurologic manifestations of anoxia were in general similar to those attributed by Levine and Schilder to inhalation of nitrogen, with the production of four phases—a stage of restless movement, a myoclonic stage, a rhythmic stage and a tonic stage. Various changes in behavior occurred. No notable improvement was seen in any of the patients; on the other hand, no untoward permanent mental or physical changes were demonstrated, even with exposure to the 4.2 per cent oxygen mixture which corresponds to an altitude of approximately 31,000 feet (9,500 meters).

CHODOFF, Langley Field, Va.

NEUROTIC MANIFESTATIONS OF THE VOICE. MORRIS BRODY, Psychoanalyt. Quart. **12**:371, 1943.

Brody points out that the voice is a sensitive reflector of emotional states and is used by the ego as a vector for neurotic symptoms and defense mechanisms. To hear the voice solely for what it has to say and to overlook the voice itself deprives the analyst of an important avenue to emotional conflicts. The defensive operations of the ego are the tools with which the analyst must work; and since resistances are constantly being acted out by means of the voice, it is doubly important that such behavior be exposed and analyzed. Interpretations regarding changes in voice are usually effective because they are readily appreciated by the patient. The most difficult voices to recognize as pathologic are those arising from vigorous defensive processes in the past which have developed into permanent character traits.

PEARSON, Philadelphia.

SOME ASPECTS OF A COMPULSION NEUROSIS IN A CHANGING CIVILIZATION. HENRY LOWENFELD, Psychoanalyt. Quart. **13**:1, 1944.

There has been considerable discussion in psychoanalytic circles about the interrelationship of the problems of psychoanalysis and those of culture. There is a difference between the content of the neuroses of the present day and those described by Freud. The neuroses occurring in different epochs present very different symptomatic pictures and offer different preventive and self-curative possibilities. Freud expressed the opinion that the neurosis is a product of the great demands of civilization on man's instincts. Civilization, however, offers ever changing aids for the mechanisms of defense and channels for sublimation. Perhaps cultural development is actually motivated by man's endless need for help in his struggle with his instincts. In the well balanced society depicted by Freud in his earlier writings the main task of analysis was to bring neurotic conflicts into consciousness. If the patient recognized that his anxieties and their projection into the world were based on childhood distortions of reality, he would find his normal place in a balanced world. The lifting of repressions was the decisive factor, because the ideals of civilization supported the ego in its struggles with the instincts. Today this secure social basis has vanished. Social reality, instead of being a standard for the correction of the fantasies of the unconscious, is now a constant provocation for these fantasies. The chaotic condition of society and the tensions expressed in the battles of nations are like a mighty breaking forth of instincts from their civilized domesticated and sublimated forms. Adults, in their attitudes toward nature, the cosmos and society, were protected formerly against a feeling of childhood helplessness by trust in God, by pantheistic

experiences and by belief in scientific progress. In a society in which institutions and their meaning are changing, homosexual sublimations tend to break down, because homosexuality in its sublimated form plays an important role in social relations and in the structure of society.

When reality becomes a provocation to the unconscious, its role in overcoming anxiety is altered, because the ego is compelled to ward off external situations which provoke forbidden unconscious wishes. Social theories which were originally developed for the purpose of understanding and mastering reality now replace cognition and take over the function of warding off the threat and provocation of reality; they become defense mechanisms. When these theories threaten to lose their protective character, they must by compulsion be maintained, so that the end result is no longer a cognition, but, rather, a repudiation, of reality. Different epochs offer a man various methods of overcoming the problems arising from his biologic instincts. He seems to need certain general concepts to make it possible for him to keep his equilibrium in the difficult situations between danger and instinct. These concepts contain his childhood problems and offer solutions for them. In epochs of cultural stability the tensions reach a balance, and the person lives out his childhood conflict in later life in a more objective way. As long as the adult struggled above all with the unknown and the dangerous in nature and the cosmos, the religious concept proved a satisfying solution. When these solutions, or their derivations, lost their force, the solution of conflicts in a sublimated form became more difficult, and man was driven to instinctual outbreaks, neurotic reactions and specific defense mechanisms. The struggle with man-made civilization led to the formation of theories and ideologies which have the same functions as religious concepts but can fulfil these functions only insufficiently because they are constantly endangered by reality. The functional background of such ideologies is difficult to penetrate because they represent a normal attempt at a solution, because at the present stage of civilization they seem to be rational and because analysts themselves participate in such ideologies.

PEARSON, Philadelphia.

GASTRODUODENAL DISORDERS. WILLIAM H. DUNN, War Med. **2**:967 (Nov.) 1942.

Dunn reviews the literature, particularly the British, on gastroduodenal disorders in military patients. These constitute the most important medical problem of the war and the most prevalent disease in soldiers. In over 50 per cent of cases the disturbance is said to be due to peptic ulcer.

The frequency of gastroduodenal disorders appears to be related to the inadequate screening of the recruits with a history of ulcer or with a pronounced neurotic personality structure. One may anticipate that patients with such a disorder will be one of two types: (1) men with driving ambitions and a high sense of responsibility, who have a strong desire to enter the service but who are inclined to worry about their home responsibilities, and (2) men with a somewhat hysterical personality structure who are strongly attached to their families and are often characterized as "mama's boy."

A contributory factor to the development of gastroduodenal disorder is the prolonged state of tension which arises in men mobilized for war and exposed to hostile action, with little opportunity to strike back.

PEARSON, Philadelphia

TROPICAL NEUROPSYCHIATRY. JAMES L. MCCARTNEY, War Med. **3**:351 (April) 1943.

Fifty per cent of tropical diseases are parasitic in origin and therefore are not likely to be transplanted to the United States because the climate here is unfavorable to the parasite hosts. The other 50 per cent are known to have neurologic sequelae, and it was recognized in times past that residence in the tropics often had a permanent effect on the personality. Thirty-six per cent of American missionaries were furloughed home because of neuropsychiatric problems, and the various nations who maintained armed forces or business offices in the tropics have insisted on only a short tour of duty in tropical climates for their employees and soldiers.

There is a strong probability, therefore, that many members of the American armed forces will be invalided from tropical duty because of neuropsychiatric effects of their tropical residence. They will show the effects of some of the following conditions:

1. Residence in the tropics sooner or later causes a reduction in blood pressure and in the basal metabolic rate, as a result of the excessive heat and the light of the sun.

2. The excessive light of the sun may result in the development of night blindness.

3. Neurasthenia is common in the tropics. Some authors believe it is the result of the excessive sunlight because it is worse among blondes, but undoubtedly it is due also to the different milieu. In the tropics moral standards are lower; human values are not worth mentioning, and intemperances of every kind are the order of the day. Sexual promiscuity is to be found everywhere, and as a result psychic conflicts and guilt feelings are set up in the white man's conscience, particularly as at first the sexual system is stimulated by the climatic conditions. The neurasthenic person attempts to overcome his unpleasant feelings by overindulgence in stimulants. The white man in the tropics has a great danger of becoming neurasthenic and, secondarily, of becoming chronically addicted to alcohol.

4. The effects of alcohol are more severe in the tropics. Korsakoff's syndrome and delirium tremens are more frequent there than in temperate climates.

5. The use of alcoholic beverages, with the natural limitation of diet which it causes and which results also from the fear of intestinal infection, frequently leads to vitamin deficiencies. Vitamins A, C and B are those most deficient in the tropics, lack of vitamin B causing beriberi, pellagra, anemia and multiple neuritis.

6. Dietary intoxications, such as lathyrism, and food poisoning, cysticercosis and dysenteries, are common. The last-mentioned condition may result in displacement of the libido from the genital to the anal zone.

7. Neurologic sequelae often follow infection with worms and flukes. Trypanosomiasis, malaria, leprosy, relapsing fever and dengue all cause involvement of the central nervous system, with neurologic signs and changes in personality as frequent sequelae.

8. Although syphilis is common, tabes and dementia paralytica are rare.

9. There are many psychic reactions to tropical diseases similar to those in temperate climates and based on the same unconscious conflicts. Many of these sequelae, and many of the diseases themselves, could be prevented by insistence on precautions in personal hygiene and by preparing soldiers and sailors for meeting the moral hazards of tropical life.

PEARSON, Philadelphia.

ETIOLOGIC FACTORS IN THE ADJUSTMENT OF MEN IN THE ARMED FORCES. DAVID LOUIS STEINBERG and MARY PHYLLIS WITTMAN, War Med. **4**:129 (Aug.) 1943.

Steinberg and Wittman report the results of a differential study of sociologic, developmental, personality and adjustment characteristics of 158 men attached to the medical corps. The subjects included 22 patients, chiefly psychoneurotic, in a psychiatric unit and 87 patients, largely psychotic, who had been discharged from the Army within the past year and a half and were now in the veterans' unit of a state hospital.

A battery of tests, including the Elgin developmental history, the Guilford personality scale and the Bell adjustment inventory, was used.

The personnel of the medical corps unit and the patients in the psychiatric unit had an educational level approximately that of graduation from high school, while that of the patients in the state hospital was lower. The length of military service was longer in the control groups than in the two groups of patients studied. Subjects in civilian life held two or three times as many positions as did the subjects in the control groups. Moderate drinking was most frequent in the control groups, while total abstinence and infrequent drinking occurred more often among the patients. There was a relatively higher number of divorced persons among the patients than among the control groups. The patients tended to love their mothers rather than their fathers, to have emotionally unstable mothers and to have mothers who were oversolicitous as compared with the mothers of the control group. The psychotic patients had a history of poorer adjustment during their early home life and school life than did the psychoneurotic patients or those of the control group. The psychoneurotic patients had a history of poorer adult health, social and emotional adjustment than did either the psychotic patients or the control group.

On the Guilford scale, the psychoneurotic and the psychotic patients showed a greater tendency to social introversion, depression and cyclothymia, and the control groups, a greater tendency to thinking introversion and to a care-free disposition.

The Bell scale for adults indicates levels of adjustment in five fields: health, home, social problems, emotion and occupation. On this scale the psychoneurotic group showed significantly more maladjustment in their social life than did the group of medical corps personnel.

Self evaluation of poor social and emotional adjustments in adult life characterized the psychoneurotic group, while maladjustment in the sexual and social life characterized the psychotic group.

The authors' studies indicate that a person who is characterized by strong cyclothymic reactions and traits of social introversion and depression, i. e., the person who is shy and self conscious, withdraws from social contacts and has strong emotional reactions with feelings of depression, unworthiness and guilt and tendencies to fluctuations in mood, flightiness and instability, makes a poor soldier, particularly if he has shown these symptoms before induction. The authors found an overlapping of specific etiologic factors between the psychoneurotic, psychotic and control groups, but they point out that the level of adjustment is not due to the presence or absence of any specific factor but is the result of the number and intensity of the factors.

They believe that rating forms, such as they have used, could be developed and standardized for use at classification centers and in camps to determine the status of borderline persons who are not well adjusted but are not such unquestionably poor psychologic risks as to be rejected by the induction boards. Such tests would be useful also in helping the examining psychiatrist at the induction center in his evaluation of the inductee, as it would give comparable results at various centers. If used routinely, the results of such studies would be of importance for future research.

PEARSON, Philadelphia.

REACTIVE ANXIETY AND ITS TREATMENT. G. GARMANY, Lancet **1**:7 (Jan. 1) 1944.

Garmany discusses cases of reactive anxiety in a British naval depot. The treatment is chiefly outpatient in type, patients continuing in their normal work routine. This, the author believes, is the best occupational therapy. Of 1,342 patients with this type of neurosis, 1,171, or 87.7 per cent, were returned to active duty in three months.

The author stresses the importance of distinguishing between those who are consciously, and often brazenly, avoiding duty and those who are suffering from an accumulation of greater than normal fear. The first group "never develop reactive anxiety because they never permit a conflict to develop at all. The problem they present is not a medical one and they should find no sanctuary with the psychiatrist." All treatment is based on honesty with the qualification that "there are a few occasions where an economy of truth, not inconsistent with the policy of honesty, is better therapy. With some men a degree of self-deception and permitted repression may be less wounding to the ego, and achieve a cure more quickly, than perfect clarity of insight rigorously demanded. Unjustified self-esteem may be of great assistance in rehabilitation, and should not be attacked indiscriminately."

As a first step in treatment, it should be made clear that the responsibility for cure lies with the patient. The physician helps him to get back his confidence. An ideal complete cure must not be assumed. The reality of symptoms must not be questioned by the physician, but he must impress the patient with the realization that they are not incapacitating. The quantitative difference between his present fear reaction and that which he had experienced before must also be made clear, for the author believes that the "reactive anxiety of war should be regarded as a condition pathological not in its nature but in its maintenance and continuity." From then on, treatment consists in steering carefully between too much condonement (so deteriorating to good group sense) and antagonizing disparagement. Symptomatic treatment must be vigorously employed and in nearly all cases an involved analytic approach avoided.

MCCARTER, Philadelphia.

Diseases of the Brain

UNUSUAL FORMS OF NYSTAGMUS. HENRY C. SMITH and F. REGIS RIESENMAN, Arch. Ophth. **33**:13 (Jan.) 1945.

Smith and Riesenman discuss 3 cases of unusual and comparatively rare forms of nystagmus. Two were cases of ocular nystagmus, volitional and occupational, and the third was a case of mixed nystagmus, due to compression of the upper cervical portion of the spinal cord.

Fundamentally nystagmus may be of vestibular, cerebellar, cerebral, upper cervical or ocular origin. The optic system is involved in all forms, but it is only in the ocular type that it is directly affected. In

all other forms it is involved indirectly by way of the vestibular system. The vestibular system may be the seat of origin of irritative phenomena and may transmit the abnormal impulses to the ocular system, or the pathologic change may be in the cerebrum, the cerebellum or the upper cervical portion of the cord, in which event the vestibular system, together with the posterior longitudinal fasciculus, acts as a nucleus for the mediation of the abnormal impulses. The occurrence of nystagmus with lesions of the cord is uncommon, but a review of the literature indicates that a number of cases have been reported. It is assumed that the nystagmus in the authors' case was the result of interference with the spinocerebellar pathways, resulting in abnormal stimulation of the cerebellum, which, in turn, involved the optic system.

SPAETH, Philadelphia.

CAVERNOUS ANGIOMA OF THE MEDULLA. ROQUE GRAZIANO, Rev. argent. de neurol. y psiquiat. **8**:415 (Dec.) 1943.

Graziano believes that his is the first case of cavernous angioma in the medulla oblongata reported. A 30 year old Argentinian farmer was admitted to the hospital Jan. 27, 1943 and died the next day. The illness was of six months' duration. It began with hiccups, which lasted two days and recurred two days later, this attack lasting four hours. At that time he complained of sore throat and numbness of the right side of the face and tongue. His family noted that the right palpebral fissure was wider than the left. He then began to complain of intense pain in the back of the head and of headaches and dizziness. In a few days he was unable to walk. He also had difficulty in speaking. He was hospitalized for a month. He then worked for four months in spite of headaches and dizziness; soon afterward he noted numbness of the entire right side of the body and clumsiness of the right hand. Ten days prior to admission he was sleepless and became delirious; for four days he was unable to talk, chew or swallow.

On examination the patient looked acutely ill and was confused. The right palpebral fissure was wider than the left; the jaw deviated to the right; the right pupil was smaller than the left; nystagmus was present with lateral and upward gaze; there was some diplopia; the pupillary reactions were normal and the right corneal reflex was diminished. There was atrophy of the borders of the tongue, with deviation of the tongue to the left. Nasal regurgitation occurred. There were aphonia and marked dysarthria. The response to pinprick was diminished on the left side of the face. Finger to nose ataxia was present on the left side. The knee jerks could not be obtained. There was no Babinski reflex or other confirmatory sign. The gait could not be studied. The clinical diagnosis was syringobulbia.

At autopsy a soft enlargement of the left side of the medulla was seen. A transverse section in the region of the pontobulbar junction showed an oval tumor, 1.5 by 1 cm., which was dark red and definitely delimited. The inner border reached the midline; the ventral border extended to the region of the pyramids and the dorsal to within 2 or 3 mm. of the floor of the fourth ventricle. A more caudal transverse section, at the level of the olives, showed the tumor to be larger and more irregular, extending beyond the midline and laterally to within 2 mm. of the outer border of the medulla. The tumor was apparently composed of many cavities, of various sizes, which were filled with blood. Microscopic examination showed the tumor to be composed of many dilated blood vessels, varying in size; the walls of the vessels were occasionally adherent to each other and sometimes were even torn, so that some of the cavities communicated with each other. Most of the blood vessels were separated by bands of fibrous tissue and the remains of necrobiotic bulbar parenchyma. There was no angioblastic tissue. The diagnosis was a cavernous angioma of the medulla.

SAVITSKY, New York.

Vegetative and Endocrine Systems

THE SYNDROME OF PRECOCIOUS PUBERTY, FIBROCYSTIC BONE DISEASE AND PIGMENTATION OF THE SKIN: ELEVEN YEARS' OBSERVATION OF A CASE. BERNARD M. SCHOLDER, Ann. Int. Med. **22**:105 (Jan.) 1945.

Scholder reports the case of a 19 year old girl who has been under his observation for eleven years. Delivery was attended by considerable trauma to the mother. Vaginal bleeding began suddenly in the child at the age of 3 years and recurred at irregular intervals for the next two years; since the age of 7 it has been a constant feature. Tenderness of the breasts appeared at 3 and the mammae became prominent at 4 years. At the age of 5, pubic hair appeared, and facial asymmetry became apparent. The syndrome of precocious puberty, fibrocystic changes in bone and pigmentation of the skin has been compatible with an otherwise normal life and development. Physical examination revealed slight facial asymmetry, decrease in size of the left limbs and small stature. Growth ceased at the age of 12, with a maximum of 61.5 inches (156 cm.). The results of laboratory studies were not remarkable except for an increase in the amount of "sex hormone" in the urine when the patient was 9 years of age. Roentgenographic studies have shown profound and widespread changes in bone condensation and absorption, but there has been only slight progression of these changes over the past ten years.

Scholder advances the hypothesis that the syndrome results from a hypothalamic (pituitary) parathyroid disturbance.

GUTTMAN, Philadelphia.

Society Transactions

ILLINOIS PSYCHIATRIC SOCIETY

DAVID SLIGHT, M.D., *President*

Regular Meeting, Dec. 7, 1944

Experimental Study on Treatment of Dementia Paralytica with Penicillin. DR. C. A. NEYMANN, Chicago; DR. G. HEILBRUNN, Manteno, Ill., and DR. G. P. YOUMANS, Chicago.

Intravenous and intramuscular injections of penicillin sodium over a period of one to two weeks were ineffective in the treatment of dementia paralytica because the hematoencephalic barrier could not be breached. No trace of penicillin was found in the spinal fluid regardless of whether the drug was administered in massive doses (up to 1,000,000 Oxford units of penicillin intravenously within three hours or 3,100,000 Oxford units intramuscularly over a period of one week) or whether it was given in conjunction with induction of artificial fever or with injections of bile salts.

The intracisternal route was finally chosen, but this method proved dangerous if more than 30,000 Oxford units of penicillin was injected. The daily injection of this dose intracisternally for longer than five consecutive days was also hazardous, causing encephalopathy, with rigidity of the neck, coma and convulsions.

Two of 5 patients treated with penicillin died as the result of the therapy. One patient showed clinical improvement. Examination of the spinal fluid revealed that the chronic pachymeningitis and leptomeningitis of 3 patients were favorably influenced. The syphilitic involvement of the parenchyma in the depths of the cortex, however, probably remained unchanged.

DISCUSSION

DR. FRANCIS GERTY, Chicago: This report is interesting to one like me who has had no experience in treatment with penicillin. There is no reason to be discouraged as to the results of treatment and clinical improvement on the basis of experience in 5 cases. I well remember the first patients with dementia paralytica whom I treated by induction of malarial fever, using two methods. Only 3 or 4 patients in the series improved, as I recall, and the first 2 died. Of course, I chose the patients with the worst prognosis, as I did not want to take a chance with any other kind. Penicillin therapy must be considered as a chemotherapeutic method, regardless of the origin of the material. Experience with chemotherapy of dementia paralytica has always been somewhat discouraging—the results being similar to those that Dr. Neymann and his associates have reported for penicillin therapy. The enemy has become entrenched in some way and has already caused considerable destruction. An approach by chemical warfare, apparently, does not get through to him. It reminds me of the old fable of the man who would not take off his coat when the cold wind blew hard, but who yielded to the gentle beams of the sun. It seems that fever treatment has been more effective in treating dementia paralytica because it gets at the enemy better than other methods. I should like to ask Dr. Neymann about the rate of recovery of penicillin from the urine after injection by the intraspinal route.

DR. ROBERT GRONNER, Elgin, Ill.: Why not the lumbar route instead of the more heroic cisternal route?

My associates and I have so far treated only 2 patients, and this by the intramuscular route, with a comparatively low dosage of 1,200,000 Oxford units of penicillin extended over a period of nearly one week. In spite of the apparent inability of penicillin to get through the hematoencephalic barrier, we obtained some good clinical results: Both patients showed definite improvement in their general condition and in their ability to enunciate test words which they had been unable to enunciate before treatment. In 1 patient the patellar reflexes returned, after having been absent for many years. I followed up this patient and found that the patellar reflexes had disappeared again, after three weeks, first on one side and then on both sides. I saw the patient only last week, and he was in about the same condition as before the beginning of treatment, which was given last August. He is now suffering from a typical "cord bladder." Altogether, we are under the impression that the therapy produces improvement, but apparently it could not be maintained.

Dr. Neymann and Dr. Heilbrunn are quite right in taking the more heroic attitude and giving large doses of penicillin and using various routes. However, the 2 patients we treated were men who had not deteriorated, both were active in their occupations and were making a living, so that we did not feel justified in using too heroic a method. One patient had had malarial treatment, with little improvement; the other has an aneurysm of the aorta, which precluded fever therapy.

Serologic tests did not reveal anything of importance except flattening of the colloidal gold curve and a slight decrease in the protein content of the spinal fluid. The fluid of 1 patient gave a 1 plus Wassermann reaction after completion of the treatment, after having persistently given a 4 plus reaction.

Further clinical and experimental study will be carried on at the Elgin State Hospital.

DR. F. HILLER, Chicago: Dr. Neymann and his associates emphasized the fact that the hematoencephalic barrier is not overcome by penicillin, since the drug was not found in the spinal fluid after intravenous injection. They based their method of administration of penicillin into the subarachnoid space on this observation. May I point out that the absence of penicillin in the spinal fluid would indicate only the impermeability of the blood–cerebrospinal fluid barrier to penicillin, but not that of the hematoencephalic barrier proper? It is known from experience that the permeability of the endothelium of the choroid plexus may differ from that of the pia-glia membranes and the vessel walls. Since a therapeutic substance injected into the subarachnoid space penetrates only into the superficial layers of the cortex, such a method does not appear to offer the ideal therapeutic approach, in view of the pathologic character of dementia paralytica. The process is a true syphilitic encephalitis, with inflammatory lesions predominantly in the gray substance of the cortex and the basal ganglia. One would think that such lesions could be reached with far better success by way of the blood than of the cerebrospinal fluid. To facilitate penetration into the brain tissue,

a hope which Dr. Neymann also cherishes, one may have to improve certain qualities of the penicillin. High dispersibility of particles and alkalinity of the solution may achieve penetration of the hematoencephalic barrier proper without lowering the threshold of the blood–cerebrospinal fluid barrier.

The work of Dr. Neymann and Dr. Heilbrunn is very interesting. The treatment of dementia paralytica with penicillin deserves all encouragement.

DR. C. A. NEYMANN, Chicago: We have little to add to what has been reported. Our discouraging results are due in part to the type of patients we chose for these therapeutic experiments. Perhaps now that we know something about the dosage and the immediate acute action of the drug, we can treat patients who are not quite so deteriorated.

In the future, it may be possible to employ a mordant similar to the substances used in the dyeing industry. We may be able to find a substance in which the penicillin is soluble and which, in turn, is soluble in lipids. If such a drug can be discovered, something may be accomplished with the intravenous use of penicillin. This substance simply does not penetrate the deeper layers of the parenchyma of the brain.

DR. GERT HEILBRUNN, Manteno, Ill.: In answer to Dr. Gerty, I regret that no urinalyses for the excretion of penicillin were performed. Such a study would have been particularly informative in tracing the elimination of the intrathecally administered substance. The intracisternal route was chosen to bring the drug into the most immediate contact with the brain.

I followed Dr. Gronner's discussion with great interest; especially was I glad to learn that the clinical improvement and changes in the spinal fluid of his patients corroborated our own observations. However, we did not see any amelioration of neurologic symptoms, as reported by Dr. Gronner. One of our patients, with rather typical signs of involvement of the posterior column, still has absence of the knee and ankle reflexes, a positive Abadie sign and considerable disturbance of position and vibration sense.

Dr. Gronner's favorable results and Dr. Gerty's encouraging words are a stimulus to us to continue our search for a short and effective chemotherapy for dementia paralytica.

Common Factors Precipitating Mental Symptoms in the Aged. DR. LOREN W. AVERY, Chicago.

The appearance of mental symptoms in the aged is a matter of great concern both to the physician and to the family. The tendency is for such symptoms to be looked on as an expression of senility, from which no relief may be expected. While this is frequently true, it is important to evaluate each patient's condition carefully before a poor prognosis is given. Elderly patients are especially vulnerable to toxic states, which even in the young precipitate mental symptoms. This report concerns 22 aged patients who first manifested mental changes while under medical care. The majority of them were under observation in the hospital. The psychotic manifestations were clinically those of disorientation, confusion and memory defect. Delusions and hallucinations were observed. Since these patients recovered, it is evident that they did not suffer from senility.

Hospitalization in itself may precipitate marked mental confusion, which is especially apparent at night. The confinement of the patient to a strange room in unfamiliar surroundings, frequently amounting to solitary confinement, may result in confusion. On the other hand, hospitalization in the ward more rarely is followed by such symptoms. The removal of the patient to the home nearly always results in disappearance of the confusion.

The injudicious use of sedation is a common factor in the precipitation of mental symptoms in the aged. A noisy and unmanageable patient is disturbing, whether in the home or in the hospital. The desire for nocturnal quiet is frequently responsible for the use of sedatives. The elderly patient may be given a therapeutic dose of a sedative without danger. The danger arises when it is found that such a dose has no effect and the physician attempts to gain his objective by increasing the dose. It should be borne in mind that confused and noisy states may be delirium and may be aggravated by toxic doses of sedatives. It was found that many elderly patients recovered quickly from their mental symptoms when administration of the sedative was stopped and a stimulant was substituted.

Disturbed mental states were found frequently to follow diseases of the respiratory system, especially bronchitis. Continued confinement to bed or to the house was probably a factor. Return to activity as soon as advisable usually resulted in recovery.

Disease of the heart frequently precipitates confused states in the elderly. Patients with cardiovascular disorders may suffer from a relative histanoxia of the brain. This is a toxic state, and the addition of toxic doses of a sedative may greatly enhance the effect of the circulatory disorder of the brain.

Elderly patients need to be guarded from confinement and from overmedication. They should be kept in their home surroundings as much as possible, and great effort should be made to maintain all possible activity.

DISCUSSION

DR. JOSEPH A. LUHAN, Chicago: Dr. David Rothschild, of Worcester, Mass., in a number of clinical and neuropathologic studies, has considered the problem whether the amount and situation of damage to the brain, as disclosed by anatomically demonstrable cerebral lesions associated with aging processes, could satisfactorily explain the mental symptoms in cases of psychoses with arteriosclerosis and senility. He found, especially in the arteriosclerotic group, numerous inconsistencies between the extent of the cerebral lesions and the severity of the mental symptoms—both disturbance of behavior with little demonstrable neuropathologic change and mild mental alterations with severe cerebral damage. I myself have been impressed for years with the observation at autopsy of severe cerebral arteriosclerosis in general hospital patients who had shown no obvious mental disorder. With the lengthening of the life span, through the advance and application of medical knowledge, especially in the control and treatment of infectious diseases, the degenerative disease processes and geriatric psychiatry will assume increasing importance. Yet it has been common practice in state hospitals to accept, without staff presentation or review, the diagnosis of psychosis with cerebral arteriosclerosis or senility made on the patient's admission since these illnesses connote a progressive course and hopeless outcome. Apparently, however, functional or recoverable psychoses may occur in older people. Most physicians have encountered psychoses, especially toxic-delirious states, in older people, as well as episodes with an affective or schizophrenic reaction pattern followed by practical recovery, which, because of the age of the patient or the presence of arteriosclerosis, with or without hypertension, were diagnosed as senile or arteriosclerotic in type. With

the presence of dementia, the diagnosis of senile or arteriosclerotic psychosis is justifiable, although in the acute confusional behavior of a toxic-delirious reaction the determination whether dementia is obscured or concealed by the psychosis may have to await the natural evolution of the illness.

Just as in Rothschild's opinion, persons who are handicapped psychologically (in their personality make-up or by unusual situational strains) are highly vulnerable to arteriosclerotic psychosis, so senile and arteriosclerotic persons are more vulnerable to situational and toxic influences. However, the prognosis for the latter is often better than the connotation which the diagnosis of senile and arteriosclerotic psychosis carries. In the interests of scientific nosology, the present classifications of psychoses with cerebral arteriosclerosis and senility should be reevaluated.

As a case in point, I recall an instance in which I was called to see a 66 year old retired, successful industrialist who had become overtly psychotic about three weeks after an automobile accident in which he had suffered minor physical injuries without any evidence of head injury, but as a result of which his wife was seriously injured. He appeared restless, agitated and fearful and said that the Catholic sisters in the hospital put him under hypnotic influences and that his son-in-law had tried to kill him. He feared that his food was being poisoned. He was largely disoriented for time. There was considerable retinal arteriosclerosis; the blood pressure was 170 systolic and 90 diastolic, and the deep reflexes were greatly exaggerated. He had shown tremor of the hands for the past two years. There was a history of abnormal forgetfulness for recent events of several months' duration. I made a diagnosis of psychosis with cerebral arteriosclerosis. Since the patient had been given bromides in moderate doses by his family physician, the blood was subsequently examined for bromides and found to contain 165 mg. of sodium bromide per hundred cubic centimeters. The patient recovered from his overt psychotic reaction in a month. This occurred early in 1938, and the man has remained practically well since and able to manage his own affairs. This case represents a toxic reaction to bromides in an arteriosclerotic setting.

Then there are the cases like that of a woman aged 56, first examined early in 1943, who then had evanescent focal neurologic manifestations of hypertensive and arteriosclerotic encephalopathy, with a blood pressure of about 250 systolic and 140 diastolic. She had a history of hypertension, with a systolic blood pressure reaching to 290 mm. during the preceding five years. She subsequently became obviously psychotic with a depression, for the first time in her life, early in 1943, and recovered after eight electric shock treatments. At present she is apparently mentally well, manages her home and does her own housework, although the blood pressure has not diminished. Is this case one of psychosis with cerebral arteriosclerosis?

Dr. Victor Gonda, Chicago: Dr. Avery is to be congratulated on bringing up this important subject. In contradistinction to his observations, one must consider the fact that many elderly patients manifest psychotic symptoms in their homes, where they often become unmanageable. As soon as they are hospitalized, their symptoms disappear, with or without the use of sedatives.

There are also patients with senile dementia who show extreme restlessness or signs of tormenting anxiety, making their lives and those of their relatives miserable. Hospitalization is necessary, and despite increasingly large doses of sedatives the patient's condition remains unchanged. It is heart breaking to witness the mental sufferings. These patients are usually of advanced age, with hypertension and unmistakable signs of arteriosclerosis.

One hesitates to use electrically induced convulsive therapy with these patients. However, I can recall several instances in which the convulsive treatment eliminated the mental agony. There was left, perhaps, a person who appeared calm but was demented, or, as in another instance, the patient became socially adjusted and was able to perform some type of work for many years. An illustrative case follows:

A patient aged 74, the mother of 6 healthy sons, gradually manifested all the classic signs of senile dementia. This condition soon became complicated with a morbid fear complex, namely, that her sons would be run over by a vehicle. For two years, all day and most of the night, she stood in horror at the window of her home, watching for the "impending death" of her sons. She became greatly emaciated; because of her precarious condition and the presence of arteriosclerosis, we hesitated to give the convulsive treatment, explaining the dangers to the members of her family. The children, however, among them highly educated men, gave their permission, knowing that some serious complication might occur. A short series of electrically induced convulsions completely removed the anxiety syndrome. No complications ensued, and for all practical purposes the patient is healthy and has performed her household duties for the last three years. Her arteriosclerosis is still present.

I could cite many similar cases. This discussion should impress members of the medical profession with the fact that in cases of seemingly hopeless "senile dementia" one cannot predict which symptoms can be removed and that in such cases the convulsive shock treatment is worth a trial, in the hope that the mental suffering of the patient will be eliminated.

Dr. Meyer Solomon, Chicago: I was glad to hear Dr. Avery's paper, based on his sound clinical experience.

I believe that in the diagnosis of mental conditions in aged persons, psychiatrists have too frequently been pessimistic and have destroyed the morale of the patient and of the family without foundation.

There is a tendency when a patient is in the 60's or 70's to diagnose his mental disorder, offhand, as senile dementia. In my own practice I have held firmly to the view that even if the patient is 70 or 75 years of age his condition is not necessarily due to senile changes in the brain.

Although in a certain number of cases such disorders are due to organic disease of the brain, one should be careful in making the diagnosis of senile dementia and should be especially careful in giving a bad or a hopeless prognosis too quickly.

It is questionable whether the term "senile dementia" should not be eliminated. Even if the aged person has a progressive deteriorating psychosis, it seems to me that it would be better to use the term "progressive geriopsychosis." A geriopsychosis may be progressive or nonprogressive.

Two illustrative cases support Dr. Avery's conclusions.

About two years ago a physician called me in consultation to see a patient whose psychosis he had diagnosed as senile dementia and whom it was desired to have committed to a state hospital. The patient was confused; he staggered about, had fallen out of bed and was irritable and noisy. The history showed

clearly that he had had transient insomnia and had been placed under treatment with large doses of phenobarbital and that his condition was probably phenobarbital intoxication. Phenobarbital medication was discontinued, and the symptoms cleared up quickly.

In contrast, I was called recently to see a patient whose psychosis also had been diagnosed as senile dementia. In looking over the hospital record carefully, I found that the patient had had a period of insomnia, due to a number of factors, and that the poor sleep had produced an exhaustion psychosis. She had been placed under treatment with small and inefficient doses of a hypnotic. She was then given sufficiently large doses of a hypnotic to insure sound sleep; in about a week her condition had cleared up, and she was transferred to a home for convalescents.

Often the treatment becomes the disease. The patient is upset; excessive doses of a medicament are given, with resulting mental confusion, and a vicious circle results. It is well to remember that aged persons may have mental disorders, such as toxic conditions and cerebral tumor.

Important, and often overlooked in aged persons, are nonorganic psychoses due to emotional problems centered about poverty, lack of a suitable home, lack of attention and love, lack of occupation and goals and a host of similar psychologic factors.

In addition to the use of any medication indicated, these personal problems must be considered and attempts made to solve them.

We psychiatrists need to make a careful reevaluation of our attitudes toward old people and of the too hurried diagnosis and management of their mental disorders.

DR. LOREN AVERY, Chicago: I wish to thank Dr. Luhan, Dr. Solomon and Dr. Gonda. I think that a careful study of such patients would show that they suffered from delirium. Because of their age, this delirium took on the characteristics of senility. Dr. Solomon brought up the important question of the emotional needs of the aged person. The worst problem for the aged is the lack of anticipation. If he is able to live as though life were endless and continues to plan and to anticipate the future, he is much less likely to suffer mental changes. His ability to live in this manner depends, of course, on his physical equipment and on the responsibilities placed on him.

Dr. Gonda raises the question of whether or not the mental symptoms returned. Of the 22 patients, I was able to follow 17. Eight of them later suffered from a typical dementia and died. Four patients are known to be living and do not show serious senile changes. One patient died of cardiovascular disease with pneumonia.

Arteriosclerosis has been considered the cause of many of the mental changes seen in the aged. It is wise to remember that arteriosclerosis is the privilege of the aged and is not necessarily the basis of their illness.

Hysterical Convulsions Treated with Hypnosis and Psychotherapy: Report of a Case.

DR. BORIS URY, Chicago.

A 17 year old white girl was first seen in the dispensary of the Illinois Neuropsychiatric Institute in May 1944. The presenting symptom was a generalized muscular disorder in which the patient would lift her pelvis from the chair in a jerking movement. The movement would then radiate through the entire body, throwing her arms and legs outward. These movements had no athetoid or choreiform characteristics and occurred rhythmically at regular intervals. They were not under the patient's conscious control, and there was a history that the disturbance became greatly intensified under any emotional stress.

According to the history given by the family, these movements had begun in September 1943 and had become increasingly severe since that time. Because of her illness, she could not go to school, was excluded from most social activities and, for the last nine months preceding admission, had been kept in bed for supposed chorea.

Since the examination on her admission disclosed no indication of organic disease, the patient was hospitalized with the tentative diagnosis of conversion hysteria. More extensive hospitalization in the ward supported the diagnosis made on admission. Despite the history of chorea, the electrocardiogram was within normal limits. The results of electroencephalographic studies were also normal.

One week after her admission, exploration with sodium amytal revealed the more superficial psychodynamics of the illness. There was much conflict over sexuality, and the patient then revealed that in her behavior she was reacting to specific bodily sensations. As she described it, this sensation was "a funny sensation at the bottom of my spine which goes between my legs. It feels like it is going to be a tickle, but it isn't." The patient then revealed her rigid and distorted ideas concerning sexuality. She denied having any knowledge of the mechanics of the sexual act and thought that pregnancy could be induced by kissing. The patient also discussed her strict moral code. She did not believe in smoking, drinking or dancing, since these were interdicted by her religious beliefs. The patient and her family belonged to a conservative Baptist church, where the minister frequently preached sermons in which the previously mentioned activities were denounced as sinful. In addition, there was a verified history that the patient had been molested several years earlier by an elderly man with evident sexual intent.

At the conclusion of the initial exploration with sodium amytal, the patient exhibited a severe emotional disturbance with pronounced activation of the muscular symptoms. There was much pelvic movement, interspersed with episodes in which the patient assumed the classic *arc de circle* of Charcot. It was at this point that hypnotic suggestion was used to control the patient, with subsidence of the somatic and emotional symptoms.

Therapy was later continued with the combined use of hypnosis and free association, in which much of the dynamic material previously suggested was worked over in greater detail. Finally, the patient became sufficiently confident in her relation to the therapeutist to introduce a new emotional motif, which was to become increasingly important. This concerned her anger and resentment against her home situation, which had barred her from many of the social activities usual to a girl of her age and status.

Beginning on June 19, the patient's behavior changed markedly. Previous to this, she had been presented before several classes, where her convulsive disorder was reproduced by hypnotic suggestion. At this time the patient became more and more disturbed, and this disturbance was manifested by spontaneous return of the motor symptoms. On June 23 there developed a major hysterical episode, the content of which was of unusual theoretic interest. The patient's motor symptoms resembled status epilepticus. There were gross and rhymthic jerkings of the arms and legs, opisthotonos

and respiratory arrest. Nevertheless, it was interesting to observe that there was no true extensor rigidity and no tonic and clonic phase and that during the rigidity the arms were kept flexed across the chest. There were no synchronous dilatation of the pupils, no loss of the corneal reflex, no Babinski sign and no cyanosis. Judged by her responses, the patient was in a semi-detached state, with partial consciousness of her acting out.

It was noted that any attempt to bring the symptoms under control only aggravated their intensity. The patient was placed in a tub, where she thrashed about violently, splashing every one in the vicinity. It was therefore decided to bring her under control by hypnotic suggestion.

This process lasted about an hour and a half, during which an interesting sequence of events was revealed. Under constant hypnotic suggestion reenforced by slow massage of the eyeballs, the symptoms of the "epileptic type of seizure" gradually became less intense. As the affect began to subside and she became more conscious, the aggressiveness and temper tantrums became more evident. The patient's expression became a clear picture of primitive hate and rage. She made rage sounds, such as incomplete articulations, and the movements became disorganized from their "epileptic character" and were more and more an aimless thrashing about. Finally, after about an hour and a half, the patient became completely quiet, and her face assumed an almost beatific expression of pure dependence and passivity. Her face became smooth, calm and childlike. Before this stage was reached, she expressed her resentment at having her will broken by that of the therapeutist by several times bursting into tears, especially when supraorbital pressure was applied to stop the convulsive movements.

The patient was then removed from a hypnotic state and psychotherapy initiated with the patient fully conscious. Following the cue given by the patient's behavior, the psychiatrist encouraged her to verbalize her various resentments. The patient then revealed the fact that she had been seen by her mother two days previously, who had stated, "I do not want you to come home as long as you are jerking; I want you to stay here even if it takes a year." The patient reacted to this with much resentment. She also felt frustrated in not receiving as much attention from the therapeutist as previously. The psychiatrist was now able to bring out much of her resentment against her home environment, where all forms of amusement, such as dancing, shows and easy social relations between young people, were interdicted on the basis of religious teachings.

After this episode, there occurred minor repetitions of similar disturbances, which gradually subsided by virtue of the more consistent psychotherapy, which, as before, combined hypnosis and free association. On July 14 the patient's second sister died of tuberculosis, and after this the patient presented a dream which seemed related to the basic mechanisms involved in the determination of the form of the illness. This involved the patient's unconscious manipulation of her "body image."

"I dreamt that my sister was dead. She was lying in a coffin; then she began to pop up like she was playing 'peek-a-boo.' I knew she was dead, but she was still active. The feeling I have about this is that the person may be dead but the muscular movements go on." The patient here symbolized the dissociation of the conscious personality from the expressive muscular movements of the body. It is obvious that this mirrored the hysterical situation. Asked to express her associations with this dream, the patient stated: "When a person is dead, their soul is gone. The soul is that part of the person which is very beautiful, which tries to obey, which is the best part of you. Movements mean that the body is free, can run, jump or do what it likes. Sex is a movement, and an embrace is a movement."

The patient remained in the hospital until August. On her return to her own home and community, her adjustment showed decided improvement in that she was now sufficiently free of her disturbing muscular movements to go to school and to join in the usual social activities. There still occur occasional, moderate exacerbations under the influence of frustration, anxiety or sexual stimulation. No attempt will be made here to explore all the theoretic implications of this material, and the close resemblance of this case to some of the earlier cases of Freud is unmistakable. The dream material points to a naive, subjective concept of the body image, which certainly has some relevance to the hysterical conversion mechanism.

The prominence of rage in initiating hysterical convulsions has previously been noted by psychiatrists, who, however, on the basis of this association, have tended to interpret the genuine organic epileptic discharge as basically a rage reaction. It is a clinical fact that any affective stimulus, whether it be rage or fear, or even music, may precipitate an epileptic attack in a person who possesses the pathophysiologic mechanism. Certainly, in this patient the extreme of rage did not precipitate any organic epileptic reaction, evidence in favor of the conclusion that rage itself cannot create the essential epileptic discharge but can only influence the threshold, a possibility which, however, does not justify the equating of convulsive disorder with rage per se.

DISCUSSION

DR. MEYER SOLOMON, Chicago: I wonder whether there is not a tendency to resort too often to the more indirect and circuitous methods of examination, represented by so-called free association, so-called dream interpretation, hypnosis and barbiturates. For example, I have not been convinced that in the average case one can get any more information by studying a patient's dreams than by talking directly with him about his personal problems. In other words, is it not true that by using the direct method of approach one can in most cases get the information one needs? Frank discussion with the family and with the patient is, in most instances, quite sufficient to get the data required in ordinary clinical practice.

I do not feel that the dream interpretations given by Dr. Ury have really been proved to be correct. May one not have arrived at the heart of the problem in this case much more readily and accurately by the direct method of approach than by the indirect technics employed?

DR. C. A. NEYMANN, Chicago: Hypnosis has been employed on a larger or smaller scale ever since the days of Mesmer. It is generally recognized that the depth of hypnosis varies greatly. Physicians who have employed hypnosis frequently demand deep hypnosis to accomplish therapeutic results. The first question would, therefore, be the depth of the hypnosis. I do not consider hypnosis very deep unless the patient is absolutely anesthetic to pinprick and to more serious trauma. A thoroughly hypnotized patient can usually be taught to blanch an arm or to produce goose flesh of an extremity voluntarily and will be bent to the hypnotist's will to

the point where posthypnotic suggestion can be employed. However, such posthypnotic suggestions are evanescent. The patient soon forgets these suggestions and falls back into his former reaction type. Hypnosis has, therefore, often proved to be therapeutically inefficient, if not worthless.

At present, the only real medical value of this procedure seems to be in helping the patient to recover from a deep hysterical amnesia or from a hysterical aphonia. Such symptoms are in themselves so troublesome that it is valuable and proper to treat the patient in this manner in order to produce even temporary recovery. This, of course, has nothing to do with the underlying reaction type. Usually patients who have recovered from hysterical amnesia or aphonia either have another episode in a short period or produce other symptoms which make life just as difficult for them. It would seem that the employment of psychoanalysis together with hypnosis might be indicated for such a patient. In my experience, an exploratory hypnosis brings to light only problems which are very near the conscious level and are not buried in the deeper subconscious strata of the mind.

DR. FRANCIS GERTY, Chicago: If one wishes to have a shrub grow, one prunes it by cutting it back, and it seems that this happens with hysteria too. The more it is cut back superficially, the stronger it becomes. Of course, one is anxious to find a short, successful and lasting treatment for hysteria. In most attempts to find the short cut, however, it seems that immediate results of only temporary duration are secured. And almost always in a search for a short cut to the successful treatment of hysteria, one finds that hypnosis is included. I suppose that practically every physician here has at some time or other hypnotized a patient. Some have hypnotized a great many patients. In spite of this, and in spite of the fact that much has been written on hypnotism in the last one hundred and fifty years, from Mesmer to Freud, one still knows practically nothing about the internal processes concerned with the state of being hypnotized. One finds great difficulty in using it with any real measure of success in the treatment of patients. It is true that one can get results, as I have pointed out before, but they are only temporary. Freud, using hypnotism, started out with the idea of unearthing material that might help in understanding the mechanism that lay behind hysteria. He gave up the method because he thought that other means were better. Now, the only advantage that hypnosis could have, it seems to me, would be to save time. Certainly, one does not gain all of the information one wishes in the hypnotic state. Sooner or later one must drop the hypnotic part of the treatment in favor of something else. I must confine my discussion to that aspect of the matter, rather than consider the success of the method. Dr. Ury states that the girl is not cured yet. Expectation of that must be postponed to the future. He has gained some interesting information and probably could have gained that information without the hypnosis. In the process of doing this, he has probably learned much about hypnosis, but, in common with most physicians and psychiatrists of the past, I assume he has not learned much about hypnosis as it concerns the internal goings-on during the state of hypnosis.

DR. BORIS URY, Chicago: I want to thank all the discussants, and I think that everything that has been said was relevant to the problems of the case.

As to the depth of the hypnosis employed, I can only state that it was sufficient to control the symptoms, which were severe. As Dr. Gerty had stated, the situation seemed to be of an emergency nature. After all, patients have died from the somatic repercussions of a sustained hysterical disorder, and this girl was suspected of having a cardiac disorder, even if there were no frank signs of heart disease. Treatment of the acute state seemed limited to heavy sedation or hypnosis. I chose hypnosis because I thought it could be fitted into the total psychotherapeutic pattern.

Why I did not get more significant material in the hypnotic state I do not know. It may be a point of technic. It was my impression that in this case the nonhypnotic parts of the therapy were limited by the peculiar emotional configuration. I felt that the affect contained within the ego and accessible to the conscious personality was extremely thin. It was as though one encountered a structure made of tissue paper. There was no resistant structure with which one could interact so as to "work out" the conflict at a conscious level. Most of the affect seemed to be retained within the subconscious areas of the personality. This affect remained internalized and self cohesive but was released during the hysterical episodes. There remains the problem of tapping this reservoir of affect in the usual psychotherapeutic relationship. It is possible that this could be done more successfully by a woman therapeutist; or, again, it may be a problem of variation in technic.

Although I am not completely satisfied with the result of treatment, the patient's condition is much improved. She is going to school, is developing her social relationships and is no longer a social outcast, nor is she confined to bed for a supposed choreic motor disorder. Of course, she is subject to relapses, but they are not so severe as the previous illness, and the level of her adjustment indicates progressive improvement.

What interests me in the hypnotic technic is the possibility that this method might help one to understand the mind-body relationship from a more physiologic point of view. After all, here is a clear case in which the physiology of the brain is altered by emotional factors. It is known that one can change the electrical activity of the occipital cortex by hypnosis. Electroencaphalographic recording from this cortex when the patient has his eyes closed gives the "Berger rhythm," a result which testifies to the internal synchrony of the visual cortex. Now if one gives such a subject hypnotic suggestion that he is seeing, the electrical rhythm changes to the usual complex form associated with actual visual activity. Obviously, the physiology of the brain has been changed by the hypnosis.

I wonder whether this is not true of some of the other properties of the hypnotic state. It used to be thought that if one suggested to a patient that his arm was insensible and then burned him with a cigaret, he felt the pain physiologically but not consciously. Is it not possible that the patient does not feel in the physiologic sense? Perhaps the hypnotically induced mechanism actually inhibits certain physiologic mechanisms. Recent neurophysiologic work has indicated the presence of a widespread, yet finely articulated, inhibitory mechanism. This can be evoked from structures as low as the reticular formation in the brain, as shown by Magoun. This mechanism has a widespread cortical representation, also, and can be evoked from many structures between these two levels. It is possible that a combination of the dynamic studies in hypnosis with neurophysiologic studies of the brain by modern methods might advance knowledge of cerebral functions and their meaning in the psychiatric syndromes.

CHICAGO NEUROLOGICAL SOCIETY

R. P. MACKAY, M.D., *in the Chair*

Regular Meeting, Dec. 12, 1944

Use of Galvanic Tetanus and the Galvanic Tetanus Ratios in Electrodiagnosis of Lesions of Peripheral Nerves. DR. LEWIS J. POLLOCK, DR. JAMES G. GOLSETH and DR. ALEX J. ARIEFF.

It has been stated that a galvanic current is capable of producing a sustained contraction, or tetanus, of a muscle and that such a tetanic response to the galvanic current has variously been called "myotonic reaction," "galvanotonus" or "galvanic tetanization." Since, however, the tetanus results from galvanic stimulation, we propose that it be called "galvanic tetanus."

In addition, the ratio of the threshold value of current for galvanic tetanus to the rheobasis has been studied and has variously been called "polarization coefficient" or "contraction coefficient." Again, since this is the ratio of two specified values of galvanic current, we propose that the term "galvanic tetanus ratio" be adopted.

Both the threshold values of current for galvanic tetani and, in particular, the galvanic tetanus ratios give reliable information regarding the state of a muscle. Because of this, it is thought unwise to consider galvanic tetanus as simply one of the characteristic changes in the mode of contraction of muscle.

It should be pointed out at this time that the presence of edema fluid in the subcutaneous tissues may cause the rheobases and, similarly, the threshold values of current for galvanic tetani of even a denervated muscle to be exceedingly high. For this reason, one should be reluctant to make the diagnosis on these high values of current alone. In such a case of denervation, however, with accompanying edema of the subcutaneous tissues, one would find that even though these values of current are abnormally high the galvanic tetanus ratios would be either at or close to unity.

Attention is called to the fact that the response of muscle to either strong galvanic currents or progressive currents of long duration is tetanic. Similarly, the changes in these two types of stimulation, and in particular the changes in their respective ratios, parallel one another during the periods of degeneration, denervation and regeneration.

The characteristics of denervated muscle have been shown to be low rheobases, low threshold values of current for galvanic tetani and galvanic tetanus ratios either approaching or at unity. Conversely, the characteristics of regenerating muscle have been shown to be high rheobases, high threshold values of current for galvanic tetani and tetanus ratios which are rather large multiples of 1.

It follows, therefore, that when a sufficiently long period has elapsed after nerve injury or suture for the muscle to have become denervated (forty-five to sixty days) and examination with the galvanic current shows (1) high rheobases, (2) high threshold values of current for galvanic tetani and (3) high galvanic tetanus ratios, one may be certain that the muscle in question is not denervated but is regenerating.

When, on the other hand, a sufficiently long period has elapsed after nerve injury or suture for the muscle to be regenerating (ninety or more days) and examination with galvanic stimulation shows (1) low rheobases, (2) low threshold values of current for galvanic tetani and (3) low galvanic tetanus ratios, one may conclude that the muscle in question is not regenerating but that, on the other hand, it is denervated and that surgical intervention is indicated.

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Histopathologic Characteristics of Progressive Muscular Atrophy. DR. GEORGE B. HASSIN, Chicago, and DR. WILLIAM DUBLIN, Los Angeles.

Progressive muscular atrophy (myelopathic muscular atrophy), Duchenne-Aran type, is not a morbid entity but a component or a partial manifestation, as it were, of amyotrophic lateral sclerosis. Its clinical features—progressive muscular wasting, usually beginning in the hands, and unassociated with pain or sensory, genitourinary or trophic disturbances—become sooner or later complicated by bulbar and corticospinal signs, resulting in an unmistakable picture of amyotrophic lateral sclerosis. On the whole, the Duchenne-Aran form of progressive muscular atrophy is rare, and its pathologic picture has not been extensively studied. This is especially true of the condition of the muscles, to which particular attention has been paid in the study of the present case. A man aged 66 was admitted to the Pierce County Hospital, Tacoma, Wash., because of difficulty in breathing and swallowing, of four days' duration. He gave a history of general weakness and muscular wasting of four years' duration. The wasting was pronounced in the hands; the muscular tone was lost, and the tendon reflexes were absent; sensibility apparently was not disturbed. Because of the patient's precarious condition, which resulted in death twenty-four hours after his admission, serologic and other detailed laboratory examinations could not be made.

Necropsy revealed no gross changes in the brain or viscera except for cerebral edema and arteriosclerosis in the brain, kidneys and heart. The microscopic changes were as follows: reduced number of myelin fibers and ganglion cells in the ventral horns of the spinal cord, especially in the cervical and thoracic regions; mild neuroglial and microglial reactions, which were somewhat more in evidence in the white substance of the spinal cord, such as the areas of the pyramidal tracts; multiple hemorrhages in the medulla oblongata, obviously agonal, without reactive phenomena or parenchymatous cell changes; fragmentation of some cells, with formation of globules (sarcolytes); invasion of the fragmented muscle tissue by myophages (histiocytes); formation of vacuoles, harboring nuclei of indefinite origin; fatty degeneration of some muscle fibers; occasional mild proliferation of the endomysium and vascular changes in the form of endarteritis obliterans, and numerous amyloid bodies in both the gray and the white substance. In respect to many features, the changes in the muscles resembled those seen in nerve fibers undergoing degeneration and in cases of progressive muscular dystrophy. In the latter condition, however, lipomatosis and multiple connective tissue scars are the outstanding features. The endarteritis and the loss of the tendon reflexes in this case suggest syphilis as the possible cause of the atrophy, although endarteritis obliterans also occurs in arteriosclerosis, rheumatic fever and tuberculosis and the absence of tendon reflexes may have been due to the moribund condition of the patient.

The Dynamic Visual Field. DR. WARD C. HALSTEAD.

Book Reviews

Psychology of Women: Motherhood. Volume II. By Helene Deutsch, M.D. Price, $5. Pp. 498. New York: Grune & Stratton, Inc., 1945.

This book on motherhood by Helene Deutsch is the second volume of her study of the psychology of women. The first volume deals with girlhood and the female psyche from infancy to the age of adolescence. In the second volume the author gives a detailed psychoanalytic study of the essential successive life phases connected with reproductive activity of the mature woman. The complicated psychobiologic interrelationship of all stages of the reproductive function frequently leads to pathologic psychosomatic manifestations. These disturbances are often discussed and mentioned. The main emphasis, however, is placed on the demonstration of the normal female psyche.

In the first chapter the biologic and social aspects of motherhood in different cultures and societies are briefly presented. The subsequent chapters deal with the relation of motherhood and sexuality, the psychology of the sexual act, conception, pregnancy, delivery and confinement, and the first mother-child relationship. In the epilogue the period of climacterium is discussed.

Helene Deutsch distinguishes between motherhood and motherliness: "Motherhood refers to the relationship of the mother to her child as a sociologic, physiologic and emotional whole. Motherliness is a definite quality of character that stamps the woman's whole personality and is an emotional phenomenon that seems to be based on the child's need for care and its helplessness." She stresses therefore that the two types of the motherly and the unmotherly woman are not related to the fact of childbirth.

The relations between sexuality and motherliness are of a complicated nature—sometimes in harmony, at other times in disaccord—thus leading to different patterns of personality. The infantile concept of motherhood, the birth process, pregnancy, the sexual act, etc., supply the pattern for the later psychophysical aspects of motherhood in the mature woman. The great influence of unconscious trends on incidents of sterility, conception and abortion is demonstrated. The extent to which the periods of pregnancy and delivery are under the impact of psychic forces and the degree to which feelings of guilt and narcissistic, masochistic, destructive and other tendencies play a role during the course of pregnancy and delivery are emphasized.

After the physical separation of mother and child the two are reunited through the formation of a new and strong tie, which the author calls the "psychic umbilical cord." The motherly woman reaches this harmony with her offspring by directly identifying herself with the child. The growing mother-child relationship is influenced from the beginning by various psychologic forces from the mother's own childhood and environment.

The period of confinement assists the mother in overcoming the trauma of the physical separation from her child. The difficulties which may arise in connection with lactation and weaning are considered by the author to be largely of psychogenic origin.

In the discussion of the problem of unmarried mothers and illegitimate pregnancies, one is shown different types of illegitimate motherhood and the social and psychologic motives which may be present, such as passive masochistic trends, narcissistic and aggressive tendencies or the need for tenderness.

The time of the climacteric includes the last phase of motherhood, the period of grandmotherhood. The motherly woman receives this gratification at that time of her life which is otherwise under the impact of serious narcissistic frustrations. This dangerous age is called the time of "second puberty," in which the aging woman repeats her psychologic adolescence. By various methods of sublimation, such as social activities and flight into fantasy, the woman fights against the biologic trauma of that period.

The author illustrates her material by numerous examples taken from case histories and the psychiatric and anthropologic literature. The information presented is taken to a large extent from the author's own clinical experiences. Based on the fundamental principles and concepts of psychoanalysis, her findings shed new light on the feminine psychologic structure and show how the inner dynamic forces are of great importance in the life of the woman and mother. Of special interest is the understanding of the woman in the climacteric and of the adoptive mother, the latter having largely been neglected from the psychologic standpoint. This book is highly recommended as a valuable contribution.

A Bibliography of Visual Literature, 1939-1944. Compiled by John Fulton, Phebe M. Hoff and Henrietta T. Perkins. Prepared for the Committee on Aviation Medicine, Division of Medical Sciences, National Research Council Acting for the Committee on Medical Research, Office of Scientific Research and Development, Washington, D. C. Price, $3. Pp. 117. Springfield, Ill.: Charles C Thomas, Publisher, 1945.

The work of compiling this important bibliography was stimulated by the war. It was initially requested by the British Air Ministry, through its Flying Personnel Research Committee, and was subsequently done under contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Yale University.

The eye and vision have always been important in protecting man from his enemies. This is especially true in times of war. Moreover, the use of airplanes as an instrument of offensive strategy and the use of black-outs have obliged people to use their eyes under adverse and various circumstances.

This important bibliography considers visual literature under the headings of (1) anatomy and ophthalmology; (2) the physiology and psychology of vision as they are concerned with visual examination and testing; (3) the importance of ocular defects in military personnel; (4) ocular trauma in military service; (5) problems of ocular protection and goggles, and (6) the problems of illumination and visibility.

All this literature is carefully collected, and the work undoubtedly has been, and will continue to be, of great value to any person interested in the problems of vision. The volume is highly recommended as an excellent bibliography on this important subject.